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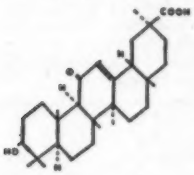

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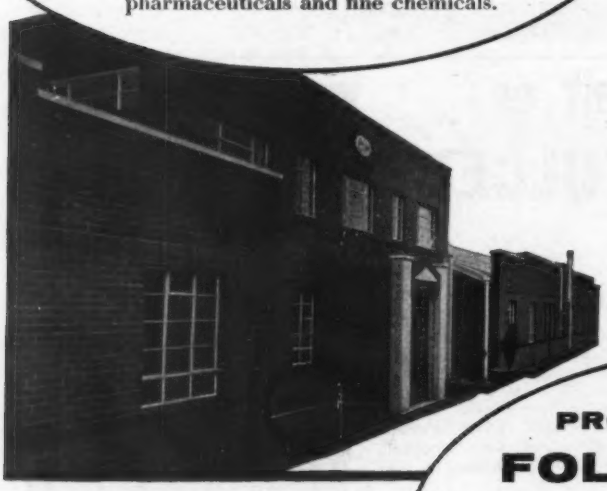

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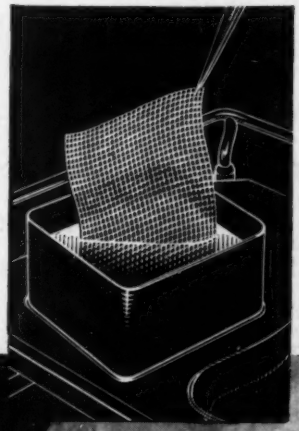

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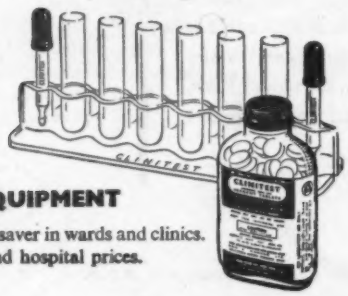

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An invaluable time-saver in wards and clinics. Write for details and hospital prices.

The advantages of ACETEST Reagent Tablets

Quick and reliable, a single tablet provides all the reagents to perform a test. Low cost permits this tablet test to be used as a screening procedure or as a routine for diabetic patients. No danger of false positives with normal urine. No caustic reagents.

TO PERFORM A TEST:

1. **Put 1 drop of urine on tablet.**
2. **Take reading at 30 seconds. Compare tablet to colour chart provided.**
3. **Record results as negative, trace, moderate or strongly positive.**

Supplied in bottles of 100 *tablets with colour scale.*

'Acetest' Reagent Tablets (*diagnostic nitroprusside tabs.*) are also available under the N.H.S. on Form E.C.10. Basic Drug Tariff price 3/10 per bottle of 100 tablets (with colour scale).

REFERENCES

(1954) 'Clinical Tests for Ketonuria', *'Lancet', April 17th, pp. 801/804*
(1954) '*Medicine Illustrated*', *May, p. 289*
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(1954) 'Clinical Tests for Ketonuria', *'Lancet', July 10th, p. 95*

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IT WAS RECENTLY reported (*Brit. med. J.*, 1: 444, 1957) that of 178 rheumatic patients, 25% could not take plain aspirin in adequate dosage.

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Not only are Paynocil tablets usually well tolerated by the stomach (even on the heavy dosage needed for rheumatoid arthritis), but they are extremely palatable, disintegrate instantly on the tongue without water, and cause no discomfort or unpleasant after-sensation.

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non-irritant, palatable, quick-dispersing aspirin

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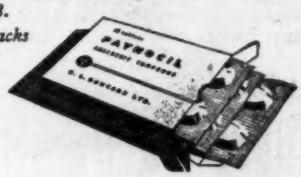
EACH TABLET CONTAINS

Acetylsalicylic acid ..... 10 grains
Aminoacetic acid..... 5 grains

PACKAGES in sealed foil strips:
Cartons of 18.
Dispensing packs of 240: basic N.H.S. cost (tax free) 21/8d.



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Detailed recommendations for dosage in rheumatoid arthritis will be gladly supplied on request

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PAEDIATRIC PRESENTATIONS

SYRUP (125 mg. per oz.): Bottles of 2 and 16 fl. oz. : SOLUBLE TABLETS (50 mg.) : Bottles of 100 · LIQUID PAEDIATRIC DROPS 1 Gram in 10 cc. bottle : FOR ORAL SUSPENSION 1.5 Gram in 1 oz. bottle: SPERSOIDS ° Dispersible Powder (50 mg. per 5 Gm.) Jars of 35 Gm. and 75 Gm.

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proved relief for "Asian 'Flu" symptoms

"A large consignment of Veganin air freighted to Hong Kong"
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rapidly reduces temperature and quickly relieves headaches

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tablets with their extra Codeine content disintegrate within 20 seconds and provide the ideally balanced formula

CAN BE PRESCRIBED ON E.C.10

Aspirin 250 mg. Phenacetin 250 mg. Codeine Phosphate 10 mg.
DOSAGE: For Asian 'Flu two tablets three times a day.

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Serious illness is inevitably followed by a frustrating period of convalescence. Metatone* with its stimulating, appetite-promoting combination of vitamin B_1 with strychnine and mineral glycerophosphates is ideally suited for the rapid restoration of normal metabolic function. It is specially valuable after 'flu and similar debilitating illnesses, after surgical operations, in neurasthenia and during pregnancy and lactation.

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Each fluid ounce of Metatone contains

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speeds the return to normal activity

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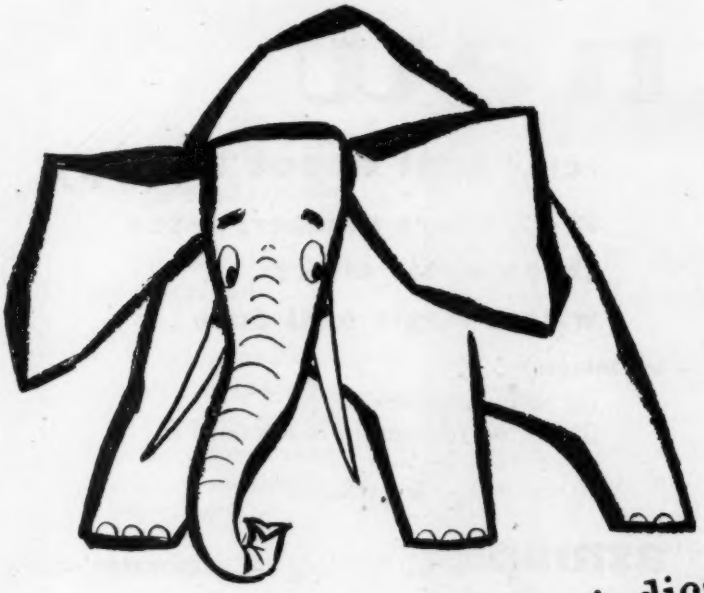
165



Where large doses are indicated . . .

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SAFE SOLUBLE ASPIRIN

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'CPL' oral depot therapy

10-12 hours uninterrupted therapeutic effect with a single oral dose

advantages:

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day-long and night-long freedom from bronchospasm

formula: ¾ gr. ephedrine hcl. (as resinate), 65 mg. theophylline, 150 mg. bromvaletone, 50 mg. mephenesin.
dosage: 1-2 tablets q 12h.
basic N.H.S. cost: 30 tablets 5/-.

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day-long appetite control
day-long mood elevation

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dosage: ½-1 tablet at breakfast time.
basic N.H.S. cost: 30 tablets 2/6.

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dosage: ½-1 tablet at breakfast time.
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In 'ionexten'-tabs. controlled ionic exchange evenly feeds the therapeutic agents into the blood stream at optimal level for 10-12 hours independent of varying physiological factors. (*'ionexten'-tabs. are not enteric coated*).

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a wise precaution . . .

"Three patients presenting radiological evidence of peptic ulcer . . .are reported . . . The apparent high incidence of this serious side effect . . . **. . . suggests the advisability of routine co-administration of an aluminium hydroxide gel".**
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The incidence of peptic ulceration following the use of prednisolone and whether or not there is a need for an antacid formulation, remains an open question . . .

. . . or a needless addition?

"Our observations indicate that prednisone and prednisolone may be used . . . without undue gastro-intestinal hazard. Further, **the addition of antacid or anti-spasmodics appears unwarranted".**
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. . . reviewing this division of opinion we have decided that, to maintain the completeness of our steroid range, we must cover both shades of opinion.

We have decided to meet these two parallel demands by offering two parallel products. Deltacortril will, of course, remain available for use where it is held that additions are unnecessary. For those who favour the use of an antacid buffer we have introduced a new product—Deltacortril (AF)—a tablet which contains prednisolone and dried aluminium hydroxide gel.

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BRAND OF PREDNISOLONE

The unmodified steroid will continue to be available in tablets containing 5 mg. and 1 mg. prednisolone.

Deltacortril* (ANTACID FORMULA)

These tablets contain, in addition to 5 mg. prednisolone, 300 mg. of dried aluminium hydroxide gel. Deltacortril (AF) is available in bottles containing 100 tablets.

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"... a state produced by intense, spontaneous neuronal activity which has a tendency to spread throughout the grey matter of the brain with unbridled augmentation ... like a prairie fire"

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EPANUTIN* (phenytoin sodium) offers four epileptics out of five the opportunity of leading normal lives. The control of seizures by this powerful anticonvulsant is achieved with negligible hypnotic effects, and is frequently accompanied by improved psychological outlook and mental alertness. Some cases of *grand mal* respond better to a combination of Epanutin and Phenobarbitone than to either of these drugs given separately.

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Epanutin Capsules (1½ grs. and ½ gr.) bottles of 100 and tins of 1,000.

Epanutin and Phenobarbitone Capsules. Each capsule contains 1½ grs. Epanutin and ½ gr. Phenobarbitone. Bottles of 100 and tins of 1,000.

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anticonvulsant with minimal hypnotic action

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Intractable
pain
Pacatal alters reaction to pain in such a way that awareness of it is much reduced.
Pacatal potentiates narcotics and analgesics.
Smaller quantities of narcotics and analgesics are required when Pacatal is prescribed and the patient supports his condition with much less distress.
Dosage:
1 tablet (25 mg.) two or three times a day
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TRADE MARK
10-(N-methyl-3-piperidylmethyl) phenothiazine
Tablets of 25 and 100 mg. strength in bottles of 50 and 500
Ampoules each containing 50 mg. in 2 ml. in boxes of 10 and 50
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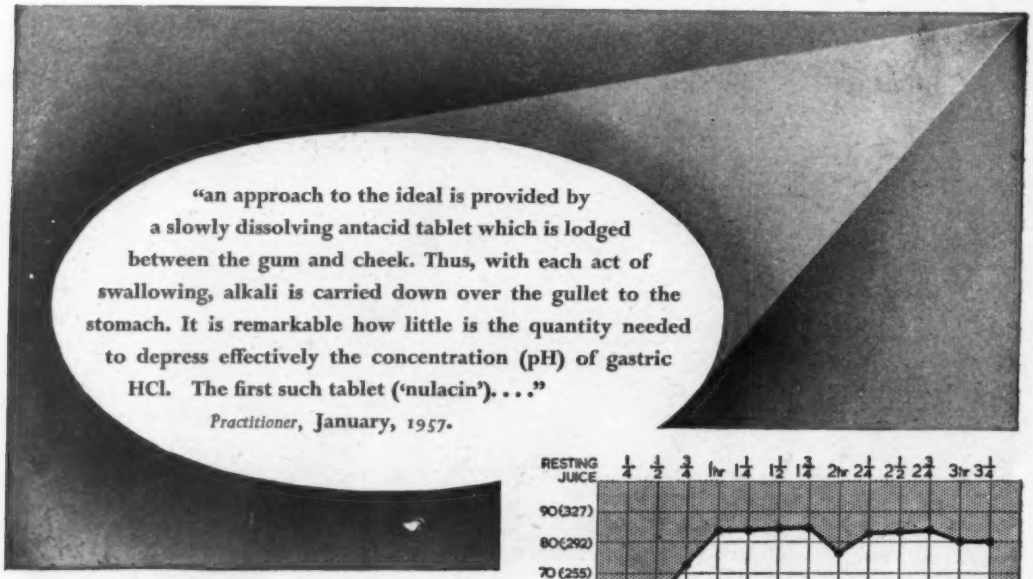
"an approach to the ideal is provided by a slowly dissolving antacid tablet which is lodged between the gum and cheek. Thus, with each act of swallowing, alkali is carried down over the gullet to the stomach. It is remarkable how little is the quantity needed to depress effectively the concentration (pH) of gastric HCl. The first such tablet ('nulacin')...."
Practitioner, January, 1957.

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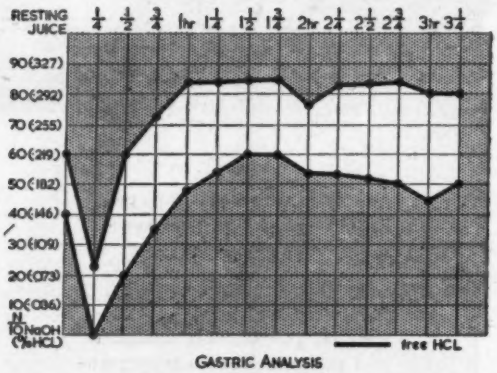
—Simple, safe, effective



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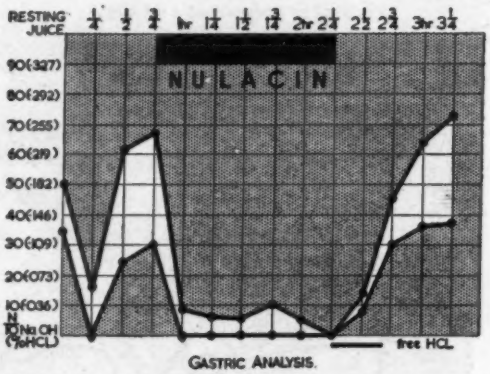
A Nulacin tablet effectively depresses the concentration of gastric HCl in peptic ulcer and other conditions of hyperacidity. It also provides protection against gastric HCl to the otherwise unprotected oesophageal wall and in such conditions as oesophagitis and hiatus hernia.

SUPPLY. Nulacin tablets may be prescribed on E.C.10. The dispensing pack of 25 tablets is free of Purchase Tax. (Basic price to N.H.S.: 2/-). Also available in tubes of 12.



GASTRIC ANALYSIS

HORLICKS LIMITED *Pharmaceutical Division, Slough, Bucks., England*

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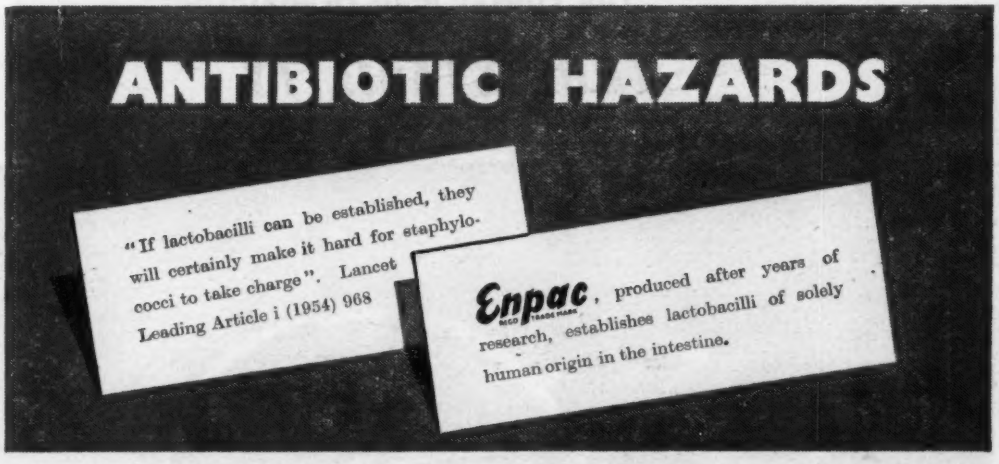
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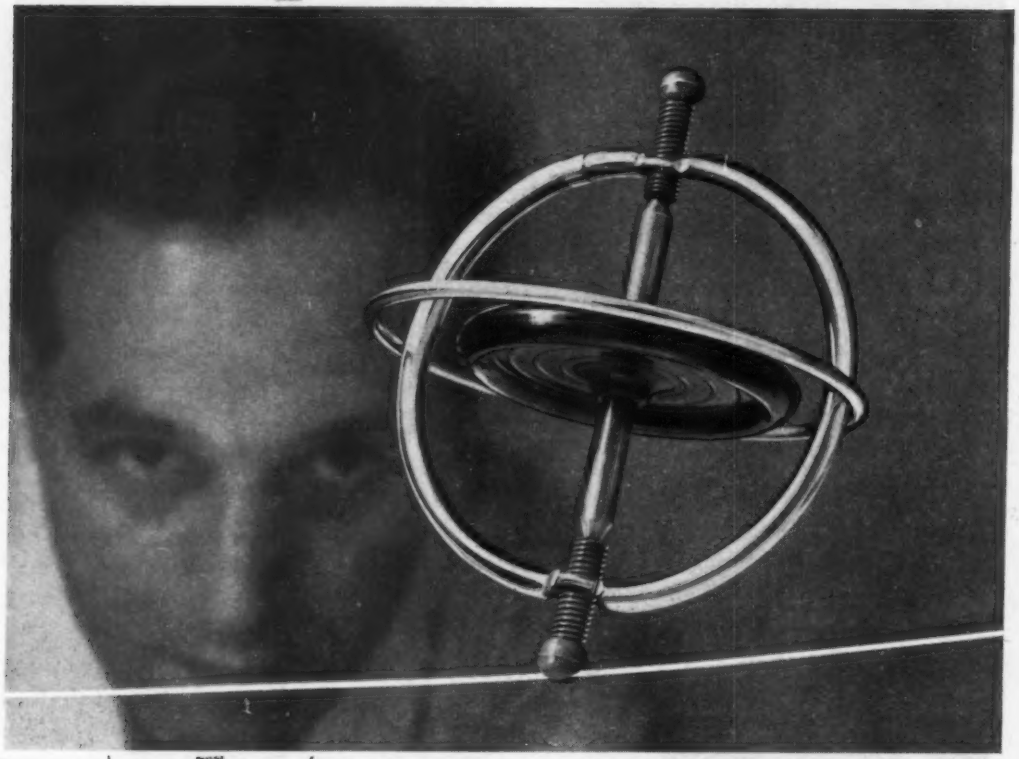
TRUE STABILITY



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especially when his father doesn't like swallowing tablets.

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Not only are the suspension and oral drop forms really pleasant to take, they
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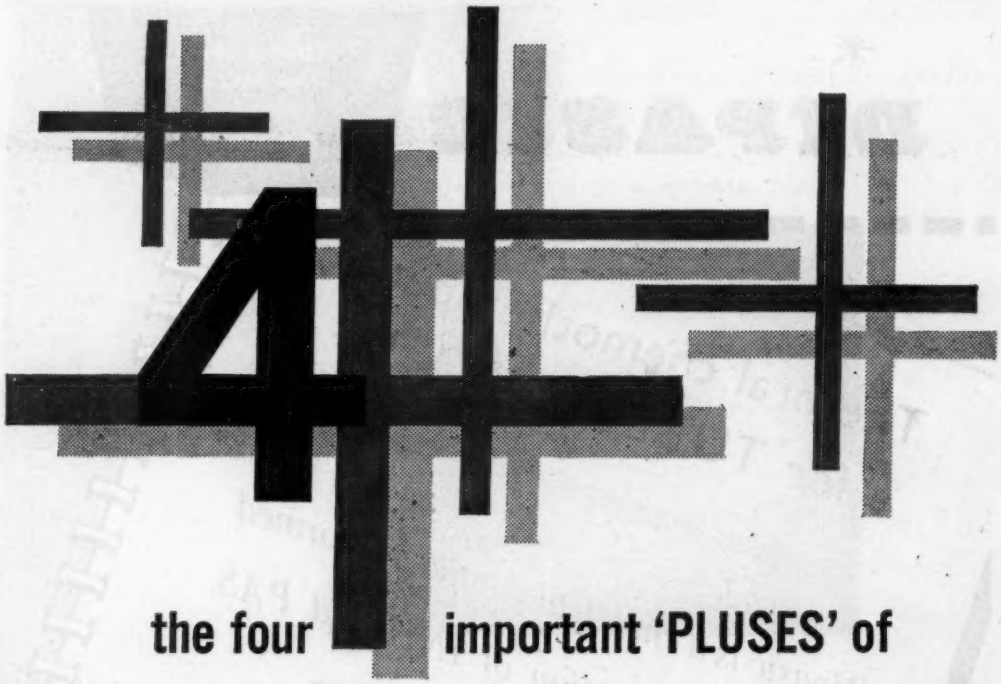

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Tablets of 100 mg. of isonicotinic acid hydrazide-p-aminosalicylate

The oral chemotherapeutic for TUBERCULOSIS

Dipasic is a chemical compound formed by the combination of INH and PAS in molecular proportions

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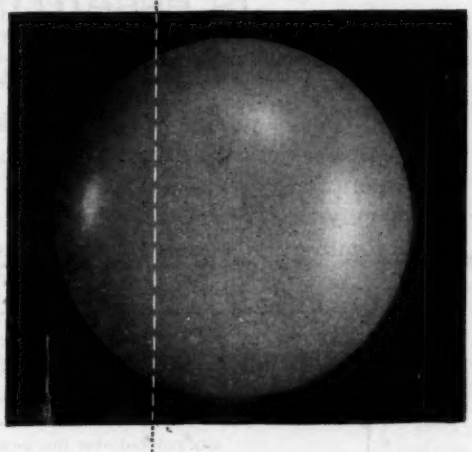

for sedation and hypnosis with **LESS** *barbiturate*

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'Rauwiloid' may require more than a week for a significant anti-hypertensive effect to develop. Any previous treatment, particularly barbiturate, should be gradually reduced over this period.

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In most cases 'Rauwiloid' will provide adequate control by itself. Combination therapy is not necessary.

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When a greater hypotensive effect is required, 'Rauwiloid' should be combined with veratrum in the form of 'Rauwiloid + Veriloid'. 'Veriloid' is a biologically standardised alkaloidal extract of Veratrum viride. Such a combination with 'Rauwiloid' enables adequate doses of veratrum to be given for a satisfactory hypotensive response. (See detailed literature).

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'Rauwiloid' used in conjunction with ganglionic blocking agents enables a smaller dose of the more potent medicament to be used, thereby minimising side-effects and decreasing the tendency for tolerance to develop.

'Rauwiloid' is available in 2 mg. tablets in bottles of 60 and 500.
Dosage, two tablets at night.

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RIKER LABORATORIES LIMITED
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"... When all aloud the wind doth blow,
And coughing drowns the parson's saw,
And birds sit brooding in the snow
And Marion's nose looks red and raw ..."

Act V. Sc. II "Love's Labour's Lost" by
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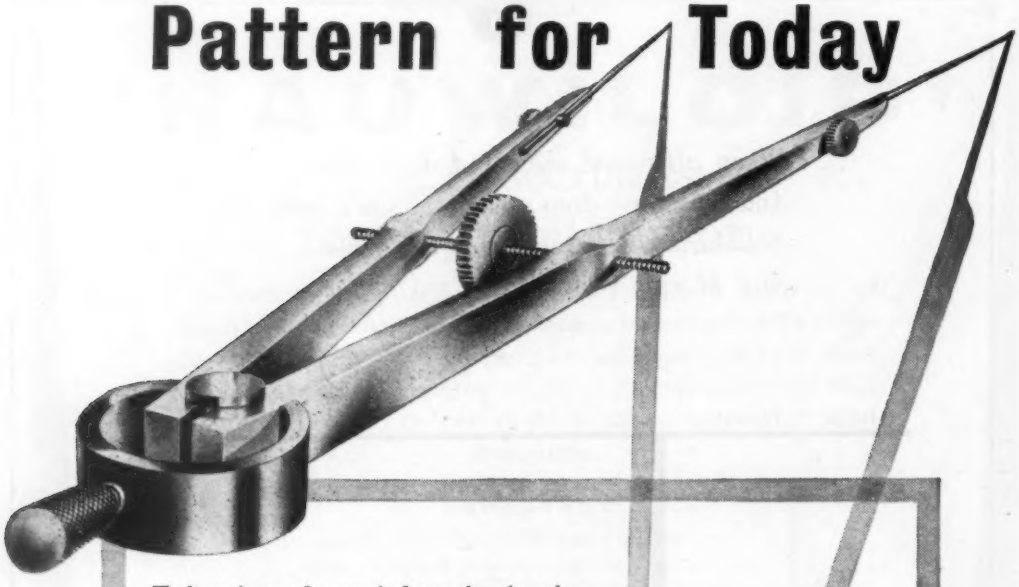

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'Pulvules'	125mg. and 250mg.
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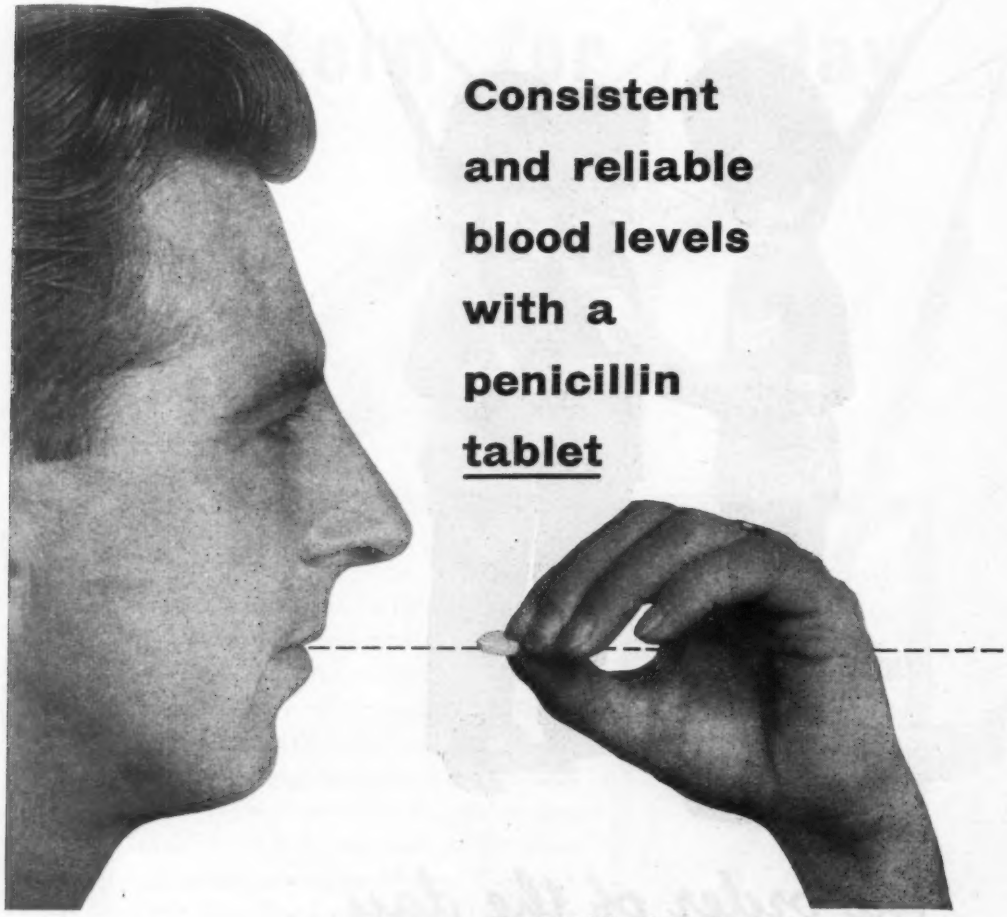

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THE MANAGEMENT OF ANASTOMOTIC ULCER

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THE results of surgical treatment of peptic ulcer are, in general, good; but anastomotic ulcer develops in about 3–5% of patients after partial gastrectomy for duodenal ulcer, and in a larger proportion after gastro-enterostomy. Doll et al. (1951) estimated that there were about 1,500,000 men with peptic ulcer in England and Wales. It is generally agreed that about 10% of ulcer patients come to gastrectomy (Walters et al. 1939, Doll 1957). Therefore at least 150,000 men have had partial gastrectomies in this country, and of these about 52% have been operated on for duodenal ulceration (Balint 1957). Hence, there may be as many as 4000 men with anastomotic ulceration in this country. The management of anastomotic ulcer is therefore an important problem. This review was undertaken to assess the various methods of treatment.

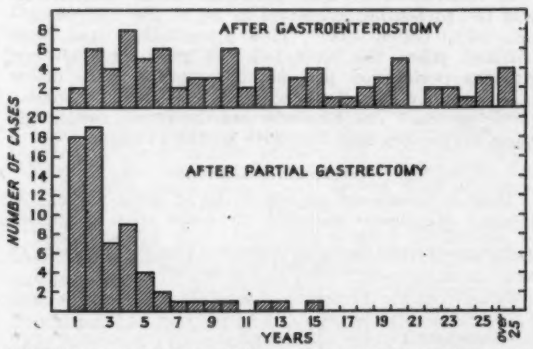
TABLE I—AGE AT FIRST OPERATION FOR ANASTOMOTIC ULCER

Age-group	No. of cases after initial gastro-enterostomy	No. of cases after initial partial gastrectomy
Under 30	2	4
30–34	4	5
35–39	7	10
40–44	21	16
45–49	10	11
50–54	15	9
55–59	8	2
60–64	6	6
65–70	9	3
Total	82	66
Never treated surgically for anastomotic ulcer	7	5
Grand total	89	71

Material

The results have been analysed of the treatment of 160 patients with anastomotic ulcer at Central Middlesex Hospital, the County Hospital, York, and St. James' Hospital, Balham. The 58 patients from Central Middlesex Hospital represent all patients admitted for treatment of anastomotic ulcer between Jan. 1, 1943, and Dec. 31, 1953. The York series of 58 patients includes all those seen in the gastric follow-up clinic between Jan. 1, 1942, and Dec. 31, 1955, while the 44 patients from Balham represent all admissions for anastomotic ulceration following partial gastrectomy between Jan. 1, 1940, and Dec. 31, 1954. The final follow-up in this series was carried out in the latter part of 1955 and early 1956. The only patients included were those admitted to hospital with radiologically or operatively proved anastomotic ulceration, following gastro-enterostomy or some form of standard partial gastrectomy. Patients with recurrent gastric or duodenal ulcers, at a distance from the anastomosis, have not been considered. In 158 cases the anastomotic ulcer had followed surgical treatment of duodenal ulcer, but in the other 2 it had followed operation for gastric ulcer.

There were 146 men and 14 women in this series. In 84 men and 5 women, anastomotic ulceration had followed gastro-enterostomy, and in 62 men and 9 women it had followed partial gastrectomy. The results of treatment in the two sexes have been similar and have therefore been considered together. The average age of these patients was 46 years. There is a rather larger proportion of patients over 50 in the post-gastro-enterostomy group (46%) than in the post-partial-gastrectomy group (30%) (table I).



Interval between initial operation and first surgical treatment for anastomotic ulcer.

The interval between the initial operation and the first surgical treatment for anastomotic ulcer varied from two months to thirty-five years and, on average, was much longer after gastro-enterostomy than partial gastrectomy (see figure). This interval was chosen because it could be measured accurately; most of the patients were admitted to hospital soon after diagnosis, and were usually operated on soon afterwards. In only 8 cases (all from Central Middlesex Hospital) did attempted medical treatment delay definitive operation for more than two years. After gastro-enterostomy the average interval was twelve years; only 10% were operated on within two years and 30% within five years. After partial gastrectomy the average interval was three years; 56% were operated on within two years and 87% within five years. One reason for the difference is that the number of gastro-enterostomies done has progressively fallen, while the number of partial gastrectomies has increased rapidly in recent years. But it is also probable that anastomotic ulceration usually arises in the first four years after partial gastrectomy, and only very rarely thereafter, whereas after gastro-enterostomy there is no

TABLE II—LENGTH OF FOLLOW-UP AFTER THE FIRST OPERATION FOR ANASTOMOTIC ULCER

Years	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Lost to follow-up
No. of cases after gastro-enterostomy	1	3	5	7	10	9	8	9	6	3	9	4	2	..	2	..	4
No. of cases after partial gastrectomy	4	12	10	10	5	5	3	4	2	5	1	1	..	..	..	1	3
Total	5	15	15	17	15	14	11	13	8	8	10	5	2	..	2	1	7

similar concentration of cases in the early postoperative years.

The average period of follow-up for the whole series was six years (table II). This was considered adequate to assess the chance of further recurrence, since 87% of anastomotic ulcers had been operated on within five years of initial partial gastrectomy.

In the 77 cases of this series for which information was available, the blood-group was O in 45 cases (58%), A in 24 (31%), B in 5 (6%), and AB in 3 (4%).

The results of gastric analyses after the initial operation have not been reviewed, for there were not reliable data in enough cases. Our impression is that such analyses are of little value in guiding treatment unless carried out with great care by experts.

It is noteworthy that gastro-intestinal hæmorrhage was the presenting symptom in 34 of the 160 cases—i.e., 20% (table III). This presentation was more common when the ulcer followed gastro-enterostomy, whereas perforation and fistula-formation were rather more common in patients with post-gastrectomy anastomotic ulcers. The numbers are, however, small, and these differences may therefore be due to chance.

Medical Treatment

Medical treatment proved to be of little value. At Central Middlesex Hospital 23 cases were diagnosed radiologically during 1953. Outpatient medical treatment, along usual lines, was tried in most of these cases, but all the patients had to be admitted to hospital for further treatment within six months. Inpatient medical treatment was equally unsuccessful (table IV).

TABLE III—INITIAL MODE OF PRESENTATION OF 160 CASES OF ANASTOMOTIC ULCERATION

Cases arising after	Presentation				
	Total	Pain	Hæmorrhage	Perforation	Gastro-colic fistula
Gastro-enterostomy	89	60	22	4	3
Partial gastrectomy	71	50	12	5	4
Total	160	110	34	9	7

Inpatient medical treatment was tried in 31 patients with anastomotic ulcer arising after gastro-enterostomy. In 24 of these the ulcer is known to have recurred, and the remaining 7 died, 4 of them from complications of anastomotic ulceration. Of 11 patients with anastomotic ulcer following partial gastrectomy treated medically, the ulcer is known to have recurred in 10. The remaining patient was well a year after treatment. Thus of a total of 42 patients only 1 is still alive and free of recurrent ulceration.

TABLE IV—RESULTS OF INITIAL INPATIENT MEDICAL TREATMENT OF ANASTOMOTIC ULCER

Cases arising after	No.	Alive at follow-up			Died	
		Recurred, operated on	Recurred, not operated on	No recurrence	Related	Unrelated
Gastro-enterostomy ..	31	21*	3	0	4	3
Partial gastrectomy	11	6	4†	1	..	..

* 2 later died of related causes: 1 after repair of gastrocolic fistula and the other after partial gastrectomy for a further recurrence.
† 3 have had repeated recurrences.

Surgical Treatment

The results of surgical treatment have been assessed by the number of recurrences, and on the basis of the Visick classification (Visick 1948). In the York series the results given were the average of several assessments. In the Central Middlesex and St. James' Hospitals series the results were based mainly on a single assessment. Because of this difference, the results shown in tables V–VIII are given as good (Visick I and II), fair (Visick III s), and poor (Visick III u and IV). The cases initially treated medically, and which failed, have been added to the appropriate surgical-treatment group.

Anastomotic Ulcer Arising After Gastro-enterostomy: First Operation

There were 82 patients in this group; the other 7 with anastomotic ulcer after gastro-enterostomy were not treated surgically. The results were disappointing, for there were many further recurrences (table V).

Polya-type partial gastrectomy was the treatment in 38 cases. Although there were 21 good results in this group, in 9 patients further anastomotic ulcers developed, and the results were poor in 5 instances.

27 patients were treated by measured radical gastrectomy (Visick 1948). There was no recurrence of anastomotic ulceration in these patients, but the results were poor in 6, and 3 patients later died, 2 of them of pulmonary tuberculosis.

Vagotomy also proved a failure. This operation was done, by the transthoracic route, in 6 patients, of whom 1 had a good result. Further anastomotic ulceration developed in the other 5 patients, and they all required further operation.

The other operations, which may be described as "palliative," all failed. Thus a perforation was sutured in 4 patients, and 1 of these died after the operation. Anastomotic ulceration recurred in the other 3 patients, and 2 of these later died of its complications. Further ulceration followed excision of ulcer in all 3 patients in whom it was done, and in the 1 whose bleeding ulcer was merely oversewn. In 2 patients a gastro-colic fistula was repaired; another anastomotic ulcer developed in 1, and the other patient could not be traced.

TABLE V—RESULTS OF FIRST SURGICAL TREATMENT OF ANASTOMOTIC ULCER ARISING AFTER GASTRO-ENTEROSTOMY

Operation	No. of cases	Results				Deaths		Lost to follow-up
		Good	Fair	Poor	Recurrences	Related	Unrelated	
Partial gastrectomy	38	21	2	5	9	..	..	1
Radical partial gastrectomy	27	12	6	6	..	..	3*	..
Vagotomy	6	1	..	..	5	..	..	..
Suture of perforation	4	..	..	..	3†	1	..	..
Excision of ulcer	3	..	..	..	3	..	..	..
Oversewing	1	..	..	..	1	..	..	..
Repair of fistula	2	..	..	..	1	..	..	1
Laparotomy	1	..	..	..	..	..	..	1
Total	82	34	8	11	22	1	3	3

* 2 died of pulmonary tuberculosis. † 2 subsequently died of complications of further recurrences.

Second Surgical Treatment

In 22 patients treated surgically for anastomotic ulceration following gastro-enterostomy, the anastomotic ulcer recurred and a second operation was done (table VI).

9 patients were treated by Polya-type partial gastrectomy. The results were good in the 4 patients whose previous anastomotic ulcer had been treated by vagotomy, but 1 died later of an unrelated cause. The prognosis was much worse, however, for the other 5 patients in this group, who had had only "palliative" surgery for the first anastomotic ulcer. 2 of them died following partial gastrectomy. In the other 3 yet further anastomotic ulcers developed, requiring repeated admissions to hospital, and 2 died from complications attributable to anastomotic ulceration. The remaining patient was eventually relieved by vagotomy (follow-up two years).

Radical partial gastrectomy was carried out with a good result in 1 patient whose first anastomotic ulcer had been treated by vagotomy. Of 2 other patients, previously treated by Polya-type partial gastrectomy for anastomotic ulceration, radical partial gastrectomy was successful in 1, but was followed by further recurrence in the other patient. This patient was finally cured by vagotomy (follow-up five years).

In 6 patients who had had Polya-type partial gastrectomies for their first anastomotic ulcers, vagotomy gave a good result in 4, and a fair result in 1. Anastomotic ulceration recurred in the remaining patient, and led to his death following repair of a gastro-colic fistula.

A perforation was sutured in 4 patients. In 2 of these the previous anastomotic ulcer had been treated by Polya-type partial gastrectomy. Further ulceration developed in 1 patient and was finally cured by vagotomy (follow-up four years), while the other man could not be traced at the time of follow-up. The other 2 patients had previously been treated by suture of a perforated anastomotic ulcer, and the ulceration recurred yet again in both of them. A Polya-type partial gastrectomy was successful in 1 of these, but the other died following gastro-enterostomy done for the relief of stomal obstruction due to anastomotic ulcer.

TABLE VI—RESULTS OF SECOND SURGICAL TREATMENT OF ANASTOMOTIC ULCER AFTER GASTRO-ENTEROSTOMY

Operation for anastomotic ulcer		No. of cases	Results				Deaths		Treatment of recurrences
Second	First		Good	Fair	Poor	Recurrences	Related	Unrelated	
P.G.	V.	4	3	..	..	..	..	1	..
	O.	5	..	..	..	3	2	..	1 : M. × 5, P.G., M.† 1 : M. × 2, V. 1 : M. × 3, P.G.†
Radical P.G.	P.G.	2	1	..	..	1	..	..	1 : V.
	V.	1	1	..	..	..	..	..	..
V.	P.G.	6	4	1	..	1	..	..	1 : R.†
S.	P.G.	2*	..	..	..	1	..	..	1 : V.
	S.	2	..	..	..	2	..	..	1 : P.G. 1 : G.†

* 1 case lost to follow-up. † Died.

G. = gastro-enterostomy, M. = medical treatment, O. = operation other than partial gastrectomy or vagotomy, P.G. = partial gastrectomy, R. = repair of gastrocolic fistula, S. = suture of perforation, V. = vagotomy.

TABLE VII—RESULTS OF FIRST SURGICAL TREATMENT OF ANASTOMOTIC ULCER AFTER PARTIAL GASTRECTOMY

Operation	No. of cases	Results				Deaths		Lost to follow-up
		Good	Fair	Poor	Recurrences	Related	Unrelated	
Partial gastrectomy ..	7	1	1	..	5	..	..	..
Radical partial gastrectomy	13	6	2	..	4	1	..	..
Partial gastrectomy with vagotomy	11	6	1	..	1	1	..	2
Vagotomy	27	13	3	5	4	..	..	2
Suture of perforation ..	6	..	..	..	5	..	..	1
Total gastrectomy ..	1	..	1	..	..	..	..	..
Laparotomy	1	..	..	..	..	1	..	..
Total	66	26	8	5	19	3	..	5

These results show that the surgical treatment of anastomotic ulcer following gastro-enterostomy is often unsatisfactory. There is, however, a suggestion in these data which might indicate a more fruitful line of surgical treatment. In this group of patients with anastomotic ulcer following gastro-enterostomy, some form of partial gastrectomy or vagotomy was used alone in 78 cases, with 18 recurrences (23%), whereas in the 14 cases where vagotomy and partial gastrectomy were both done in the same patient, there was only 1 recurrence (7%).

Anastomotic Ulcer Arising After Partial Gastrectomy : First Operation

There were 66 patients in this group; the other 5 patients with anastomotic ulcer after partial gastrectomy had no surgical treatment.

The results were again disappointing (table VII). Leaving out the 6 patients treated only by suture of a perforated ulcer (with 5 recurrences and 1 death), the 1 treated by total gastrectomy, and the 1 treated by laparotomy, there were 14 recurrences in 58 cases.

A higher Polya-type partial gastrectomy was done in 7 patients, and in 5 the operation was followed by further recurrence of anastomotic ulceration. Of the remaining 2 cases, 1 had a fair result, and the other a good result.

Radical partial gastrectomy (Visick 1948) was the treatment of 13 cases, and was successful in 6. A fair result was obtained

TABLE VIII—RESULTS OF SECOND SURGICAL TREATMENT OF ANASTOMOTIC ULCER AFTER PARTIAL GASTRECTOMY

Operation for anastomotic ulcer		No. of cases	Results				Deaths		Treatment of recurrences
Second	First		Good	Fair	Poor	Recurrences	Related	Unrelated	
P.G.	P.G.	1	..	..	..	1	..	..	1 : M., V.
	V.	3	2	..	..	1	..	..	1 : M. × 5
	S.	1	..	..	..	1	..	..	1 : P.G. + V.
V.	P.G. + V.	1	..	..	..	..	1	..	..
	S.	2	2	..	..	..	..	..	..
P.G. + V.	P.G.	1	1	..	..	..	..	..	..
	V.	1	..	..	..	1	..	..	1 : T.G.
S.G.	R.P.G.	1	1	..	..	..	..	..	..
T.G.	P.G.	2	..	2	..	..	..	..	..
En-Y.	R.P.G.	1	1	..	..	..	..	..	..
R.F.	P.G.	1	..	..	..	1	..	..	1 : V., P.G., T.G.
S.P.	S.P.	1	..	..	..	1	..	..	1 : M., P.G., T.G.

En-Y. = refashioning with en-Y. anastomosis, M. = medical treatment, P.G. = partial gastrectomy (Polya), R.P.G. = radical partial gastrectomy, S.G. = subtotal gastrectomy, S.P. = suture of perforation, T.G. = total gastrectomy, V. = vagotomy.

TABLE IX—COMPARISON OF THE RESULTS OF THE COMBINATION OF PARTIAL GASTRECTOMY AND VAGOTOMY WITH THOSE OF PARTIAL GASTRECTOMY ALONE IN THE TREATMENT OF ANASTOMOTIC ULCER FOLLOWING EITHER GASTRO-ENTEROSTOMY OR PARTIAL GASTRECTOMY (FIRST AND SECOND TREATMENTS ONLY)

Operation	No. of cases	Results				Deaths		Lost to follow-up
		Good	Fair	Poor	Recurrences	Related	Unrelated	
Partial gastrectomy and vagotomy ..	57	32	5	5	8 (14%)	1	2	4
Partial gastrectomy alone ..	97	43	11	11	25 (26%)	3	3	1

in 2 others, and 1 died after the operation. Ulceration at the anastomosis recurred in the other 4 patients.

Abdominal vagotomy, combined with a limited further gastric resection, was done in 11 patients with 1 fair and 6 good results. There was 1 postoperative death. Ulceration recurred at the stoma in only 1 patient, and 2 could not be traced at the time of follow-up.

27 patients were treated by abdominal vagotomy only, (sometimes combined with a revision of the stoma). The result was good in 13 cases, fair in 3, and poor in 5. Further anastomotic ulcers developed in 4 patients. The remaining 2 were lost from the follow-up.

Second Surgical Treatment

There were thus 19 patients in whom an anastomotic ulcer, following initial partial gastrectomy, recurred after surgical treatment. 16 of these patients have since had further operations (table VIII).

A Polya-type partial gastrectomy was the treatment of 3 patients whose previous anastomotic ulcer had been treated by vagotomy. The results were good in 2, but ulceration at the stoma recurred in 1. This latter patient has since had five periods of medical treatment and still has an anastomotic ulcer. A third gastric resection, with a Polya anastomosis, was done in 1 patient, but his ulcer recurred and was then treated medically without success. He was finally cured by vagotomy (follow-up nine years). Polya-type gastrectomy was also done in 1 other patient, in whom a previous perforated anastomotic ulcer had been treated by suture. This patient, too, developed further anastomotic ulceration, but was finally cured by a further limited resection coupled with abdominal vagotomy (follow-up two years).

Abdominal vagotomy alone (sometimes combined with refashioning of the stoma) was done in 3 patients. In 2 of these the previous perforated anastomotic ulcer had been treated by suture, and vagotomy proved successful in both. The other patient, however, whose earlier recurrence had been treated by combined vagotomy (only partial) and gastric resection, died following the operation.

2 patients were treated by combined gastric resection and abdominal vagotomy. 1 of these had previously been treated by Polya partial gastrectomy for anastomotic ulcer, and this further operation was successful. In the other patient, whose earlier anastomotic ulcer had been treated by abdominal vagotomy, a further anastomotic ulcer developed, and was treated by total gastrectomy with a fair result.

A subtotal gastrectomy proved successful in 1 patient, whose earlier anastomotic ulcer had been treated by a radical gastric resection. In 2 patients the second anastomotic ulcer was treated by total gastrectomy, both having had a Polya-type partial gastrectomy for the first. The results were fair in both. The anastomotic ulcer was excised and an en-Y anastomosis was fashioned with a good result in 1 patient, whose first anastomotic ulcer had been treated by radical partial gastrectomy.

Repair of a gastrocolic fistula was followed by further recurrence of anastomotic ulceration in a man whose earlier anastomotic ulcer had been treated by Polya partial gastrectomy. He later had an unsuccessful vagotomy, followed by an equally unsuccessful subtotal gastrectomy, and finally a total gastrectomy was required. The result of this last operation was poor, since he now has gross steatorrhœa.

Another patient was treated twice by suture for perforations of anastomotic ulcers. Anastomotic ulceration recurred after the second suture, and after a period of unsuccessful medical treatment, a further gastrectomy was done. This was followed by yet another anastomotic ulcer, and the patient has now had a total gastrectomy—too recently for assessment of the final result.

The results of surgical treatment of anastomotic ulcer after partial gastrectomy are thus discouraging. Even after a second operation, further anastomotic ulceration developed in 6 of the 15 patients so treated. As in the cases following gastro-enterostomy, however, the combination of vagotomy with partial gastrectomy has proved superior to gastric resection alone. There were 11 further recurrences (48%) in 23 cases where gastrectomy alone was used, compared with 11 recurrences (23%) in 48 where gastrectomy and vagotomy were done in the same patient (not necessarily at the same time).

In the combined series, the recurrence-rate was lower and the proportion of good results higher after the combination of the two operations in the same patient (table IV), but the differences are not statistically significant.

Discussion

The radiological diagnosis of anastomotic ulceration is difficult, and negative findings do not exclude an ulcer. Walters et al. (1955) found that only 37% of anastomotic ulcers following gastro-enterostomy, and 50% of those following partial gastrectomy, were detected radiologically. It is therefore quite possible that many patients, admitted for hæmatemesis or melæna after these operations, had anastomotic ulcers which were not recognised. Their inclusion in this series was not, however, felt to be justified. The exclusion of such cases, some of whom have no further hæmorrhages, may have made the results of medical treatment appear unduly bad.

The sex and age distribution of the cases in this series is similar to that in many previously reported. There were 146 men and 14 women, a ratio of about 10 to 1. Eusterman and Balfour (1935) reported 248 men and 28 women, a ratio of 11 to 1, while in Wright's (1934) series there were 410 men and 40 women, again a very similar distribution. Walters et al. (1955) also found a similar sex ratio. Eusterman and Balfour found that the average age of their patients was 42 years. Doran (1948) reported that the great majority of his cases were in the fifth decade. The average age of our patients was 46 years.

It has been shown (Aird et al. 1954, Clarke et al. 1955) that blood-group O is significantly more common in duodenal-ulcer patients (60%) than in the general population (47%). Peebles Brown et al. (1956) found that 70% of their 79 cases of anastomotic ulcer had group-O blood, and showed that this was significantly higher than in their duodenal-ulcer cases. This finding suggested that some inborn factor may perhaps determine the development of anastomotic ulceration. We have, however, not been able to confirm these findings in the 77 cases in this series for whom data were available. Only 45 (58%) of these patients had group-O blood. This figure agrees well with that found in duodenal-ulcer patients generally.

The mortality from anastomotic ulcer is considerable. 15 of our patients died of causes related to the ulcer itself or its surgical treatment. 4 died from complications of the ulcer, such as gastrocolic fistula or hæmorrhage, before they could be operated on.

On the basis of this series we feel that medical treatment is of little value in the management of anastomotic ulcer, having proved to be a failure in all but 1 of the 42 cases in whom it was tried. It may, however, be of temporary value where major surgical intervention is contra-indicated because of some unrelated medical condition.

There is fairly general agreement that partial gastrectomy is the treatment of choice for anastomotic ulcer

arising after gastro-enterostomy (Priestley and Gibson 1948, Ransom 1949, Stevens and Kipen 1950, Walters et al. 1955). There were 9 recurrences after 38 partial gastrectomies in this series. Radical partial gastrectomy (Visick 1948) was not followed by any recurrences in 28 cases, but the symptomatic results were not very satisfactory. Vagotomy by itself has proved a failure. We would suggest, however, that the excessively high recurrence-rate after partial gastrectomy for anastomotic ulcer after gastro-enterostomy might be reduced by the addition of an adequate vagotomy, without increasing the incidence of post-gastrectomy syndromes (table IX).

The results of further partial gastrectomy for anastomotic ulcer after an initial partial gastrectomy have been very disappointing in this series, with 9 recurrences in 20 cases. Vagotomy has, however, proved very effective. There were only 4 recurrences in 27 patients treated by abdominal vagotomy, with or without revision of the anastomosis, and only 1 recurrence in 11 patients treated by vagotomy combined with a limited gastric resection. A similar advantage of vagotomy was shown by the results of surgical treatment of the second anastomotic ulcer after vagotomy. We feel, therefore, that vagotomy, with or without a further limited gastric resection, is the treatment of choice in these cases. This view is rather more emphatic than that of Stevens and Kipen (1950) and Wells (1954), but on the same lines. It must be emphasised, however, that vagotomy, to be effective, must be complete, and there are good anatomical reasons why it should be more complete by the abdominal approach.

Even with the most careful surgical treatment, ulcers will continue to recur in a number of cases. We have not been able to find any indication from this review of how these patients can be identified. Nothing short of a total gastrectomy seems sufficient to cure these "pernicious ulcerators." On the basis of our results it seems reasonable to suggest that a total gastrectomy should be done in any patient in whom anastomotic ulcers continue to recur after adequate vagotomy and gastrectomy.

In our experience, total gastrectomy is compatible with moderately good health, and the state of patients after this operation is preferable to the recurring misery of repeated anastomotic ulceration. Furthermore, these unfortunate patients may be saved a number of useless operations.

The 2 patients with anastomotic ulceration after gastrectomy for gastric ulcer are of interest. Their original operations were done at other hospitals, so that we have no direct evidence of the original diagnosis. In view of the very great rarity of anastomotic ulcer after gastrectomy for gastric ulcer, it is reasonable to suggest that an undetected or unrecorded duodenal ulcer may have been present as well in these 2 patients.

Summary

The results of treatment of 160 patients with anastomotic ulcer following gastro-enterostomy or partial gastrectomy have been reviewed.

Medical treatment had been of little value.

For anastomotic ulcer following gastro-enterostomy, partial gastrectomy, combined with vagotomy, is suggested as the treatment of choice.

For anastomotic ulcer following partial gastrectomy, abdominal vagotomy, with or without revision of the anastomosis, or, if necessary, a limited gastric resection to remove the ulcer, is recommended.

For patients with persistently recurring anastomotic ulcers, total gastrectomy will sooner or later be necessary. We suggest that this operation should not be delayed if anastomotic ulceration recurs after adequate vagotomy and gastrectomy.

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ARREST OF ISOLATED HEART WITH POTASSIUM CITRATE

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THIS paper describes further progress in work with isolated perfused hearts which was undertaken to test the suggestion by one of us (D. G. M.) that potassium citrate might be useful for arresting the heart in a state well suited to the needs of the cardiac surgeon (Melrose et al. 1955).

Results were obtained from the hearts of 60 freshly killed rabbits and of 4 human fœtuses from therapeutic terminations of pregnancy at the 16th to 20th week. Thirty minutes to two hours elapsed between the delivery of a fœtus and the start of heart perfusion, but, as Baker (1953) has observed, hearts so treated revive remarkably rapidly. Since so few human fœtal hearts were available, the bulk of the work was with the rabbit heart. The rabbit was chosen because, under the conditions of perfusion, the reactions of its heart to many drugs are well known and appear to be similar to those of the adult human heart in situ. Further, Wearn (1939–40) has shown that the size of myocardial fibres, the ratio of fibres to capillaries, and the intercapillary distances are nearly identical in the heart of the rabbit and that of man.

The Preparation

Perfusions were by the well-known Martin-Langendorff method in which the nutrient solution is delivered at constant pressure through an aortic cannula to the heart removed from the body. The cannula is inserted distal to the aortic valve and points towards it. Perfusion fluid forces the valve shut and can only flow through the coronary circulation, finally escaping from the heart through the cut ends of the great veins and the pulmonary artery. In experiments where it was desired to collect samples of coronary perfusate after it had traversed the myocardium, but before it could come into contact with

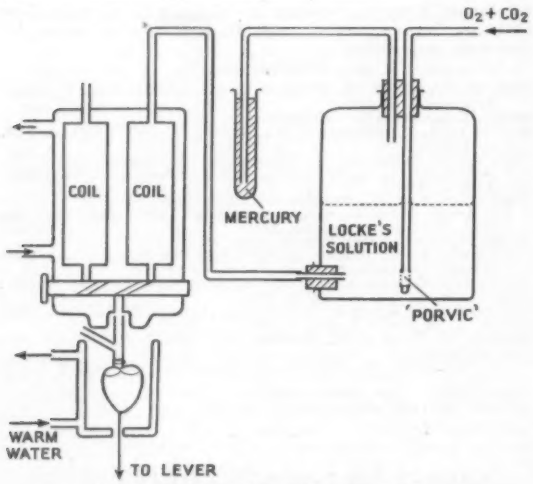

Fig. 1—Main features of perfusion apparatus.

the atmosphere, the stumps of the great veins were tied, and all the coronary effluent was collected from a cannula in the pulmonary artery.

Such perfused hearts, suspended from their aortic cannulæ, beat regularly, but with slowly diminishing force, for many hours. Although the experimental simplicity sacrifices normal circulatory function, ventricular performance may be assessed from the amplitude of beat conveniently recorded on a revolving cylinder by a spring-loaded lever attached by thread and a small hook to the ventricular apex.

The Apparatus

The apparatus is based on a previous design (Baker 1951), and the essentials are given below (see also fig. 1).

A mixture of oxygen (97%) and carbon dioxide (3%) was delivered from a cylinder to a short tube of porous polyethylene ('Porvic') closed at one end and immersed in Locke's solution in a large aspirator. (The Locke's solution consisted of NaCl 0·9%, $CaCl_2$ 0·024%, KCl 0·042%, $NaHCO_3$ 0·05%, and dextrose 0·1%.) The aspirator was connected so that excess gas mixture, after passing through the solution as a stream of very fine bubbles, could only escape to the atmosphere by forcing a mercury seal. Thus the solution was well oxygenated and was under a constant pressure; its pH was 6·9–7·0 but rose to 7·0–7·2 in the fluid on its way to the heart because warming it caused loss of dissolved carbon dioxide. A tube opening below the surface of the fluid in the aspirator led to the aortic cannula through a warming coil. There were two such coils sealed into a common warming envelope so that solutions of different composition from two aspirators could be ready for perfusing through the heart. Both coils were connected with a stopcock, also in the warmed envelope, so that the flow to the heart could be turned off either completely or from one coil at a time.

The aortic cannula, fixed into the warmed coil assembly through a rubber bung, had a side-tube which could be connected to a long vertical tube so that the perfusion pressure at the mouths of the coronary arteries could be observed and kept constant.

The cannula and the heart itself hung into the lumen of a glass jacket with double walls. Both this jacket and the warming coils were kept at a constant temperature by rapidly circulating water pumped from a thermostatically controlled bath. The jacket around the heart is essential to prevent cooling and drying, and, even in the absence of all coronary flow, maintained the temperature round the heart at whatever degree had been chosen. An aperture in the double wall at the bottom of this jacket allowed the thread from the ventricular apex to reach the recording system. Events such as heart-block and fibrillation could be observed clearly through the walls of the jacket.

Experimental Procedure

After an initial perfusion of thirty minutes with Locke's solution the perfusate was changed by means of the stopcock to Locke's solution containing a known concentration (in the case of citrates expressed as anhydrous salt) of the drug to be tested. According to the type of test required the perfusion was either left running or was stopped (coronary flow abolished) for any chosen time after cardiac arrest had taken place. At the end of this experimental period perfusion was resumed with pure Locke's solution, and the extent of recovery of the heart was noted at regular time-intervals. The degree of recovery was measured by the amplitude of ventricular contraction and expressed as a percentage of that obtaining immediately before each exposure to a drug or arrest of coronary flow. During experiments with the coronary flow interrupted by the stopcock a clip was applied to the tubing connecting the aortic cannula to the pressure-recording tube to prevent any slight perfusion from this source.

Results

RABBIT HEARTS

Recoveries after 15 Minutes' Arrest of Beat and Occlusion of Coronary Flow at 37°C

25 hearts were used, and the results are set out in table I divided into those from hearts arrested for the first time (19) and those from hearts arrested for the second to tenth time (19). 13 of the hearts in this second category were those also used in the first.

There seems to be little difference in the excellence of recovery in the two groups. This ability of hearts to recover well from repeated arrest of beat and of flow is particularly well shown by one experiment in which a heart was thus treated ten times, each for a period of fifteen minutes followed by a period of fifteen minutes on pure Locke's solution for recovery. This represents five hours of experiment, and yet the first 8 recoveries were from 91 to 100%, and the last two were 86% and 87% (fig. 2).

TABLE I—ARREST OF BEAT AND CORONARY FLOW FOR 15 MINUTES AT 37°C

	1st arrests				
No. of hearts used ..	13	1	3	1	1
Recovery of amplitude in 5–15 min.	98–100 % 2 at 5 mg. per ml.	93 %	80–87 %	62 %	0
	2nd–10th arrests				
No. of hearts used ..	13	4	3	5	..
No. of experiments ..	17	7	4	6	..
Recovery of amplitude in 5–15 min.	95–100 % 1 at 10 mg. per ml. 1 at 20 mg. per ml.	91–94 % 1 at 5 mg. per ml.	82–87 % 1 at 5 mg. per ml.	65–78 % 1 at 5 mg. per ml. 1 at 10 mg. per ml. 1 at 20 mg. per ml. 1 at 30 mg. per ml.	

Potassium citrate 1–2 mg. per ml. except where stated.

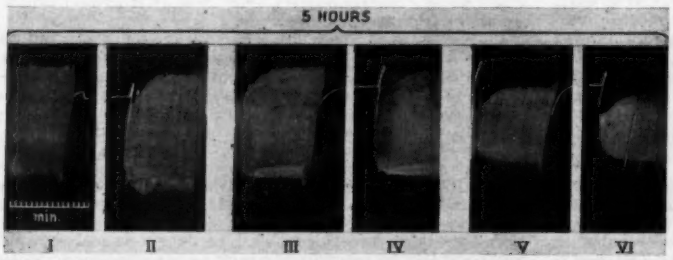

Fig. 2—Ventricular recordings of perfused rabbit heart. Systole downwards, 37°C. In I, III, and V potassium citrate 1·0 mg. per ml. in Locke's solution was perfused for 30 sec. for the first, fifth, and tenth times. Coronary flow was occluded for 15 minutes after each cardiac arrest. In II, IV, and VI are shown recoveries with pure Locke's solution. Decrement from I to VI is to be expected in five hours of experiment.

In only one instance did a heart recover with a beat so feeble that it could not be recorded. It is felt that this 1 heart, viewed against all the hearts described here, may easily represent one of those unexplained failures by no means unknown in perfusion experiments and not necessarily attributable to the injected drug or to any other deliberate procedure.

The speed of arrest varied with the concentration of potassium citrate in the perfusion fluid. At concentrations of 2 mg. per ml. and more all the hearts in this series and all the others reported here stopped in less than a minute, commonly in ten to twenty seconds. At a concentration of 1 mg. per ml. some hearts did not stop, others took one to two minutes to do so, and many stopped in less than twenty seconds. Recoveries began rapidly when perfusion was restored with pure Locke's solution. Most hearts beat again within fifteen seconds, and all except 1 within two minutes. The exception was one which took seven minutes (but recovered to 100% of its original amplitude). This heart was in a class of its own because none took nearly so long except in experiments where potassium citrate at 10–20 mg. per ml. was used and was perfused continuously during periods of arrest. No stimulants were ever needed to restore spontaneous activity.

TABLE II—ARREST OF BEAT AND CORONARY FLOW FOR 30 MINUTES AT 37°C

	1st arrests			
No. of hearts used	3	..	1	1
Recovery of amplitude in 5–15 min.	96–100%	..	74%	24%
	2nd–8th arrests			
No. of hearts used	1	4	1	1
No. of experiments	1	4	1	1
Recovery in amplitude in 5–15 min.	96%	78–84%	54%	20%

Potassium citrate 1–2 mg. per ml.

The state of the heart during arrest was typical of that induced by potassium excess or calcium deficiency—i.e., diastolic and flaccid. No escape beats were observed, and ventricular fibrillation never began during this period, though it was seen for periods of five to ten seconds during the onset of arrest in 6 of the 60 hearts reported here. In only 1 case did ventricular fibrillation come on during recovery, and then it spontaneously reverted to normal rhythm within a minute.

Recoveries all followed the same pattern—i.e., a few slow ventricular beats for about ten seconds, then sometimes a burst of tachycardia for about twenty seconds, followed by a sudden reversion to normal rhythm. The original rate of beat, or within five beats per minute of it, was regained in five to ten minutes. Detailed records of rate of beat were not kept once it was seen that ventricular rhythms or other irregularities were not the rule. It was felt that reversion to auricular control of the ventricles by normal conduction was the important observation, and that in the intact animal precise adjustment of rate would depend as usual on autonomic balance.

In 3 instances electrocardiograms were made with platinum-wire electrodes directly upon the auricular surface. It was found that, when the perfusion contained only just sufficient potassium citrate to cause complete mechanical arrest, there yet persisted some small rhythmical biphasic changes of electrical potential.

Very careful direct observations of these hearts were made in case there should still remain some mechanical activity not strong enough to move the lever recording system. No such activity was seen, even though in other hearts not quite arrested it was possible to make out very tiny movements by observing the reflections of light from the glistening surface of the posterior surface of the auricle, usually the last area to stop moving.

Recoveries after 15 Minutes without Coronary Flow at 37°C and without Previous Arrest of Beat

Only four experiments were made on 3 hearts, and the recoveries obtained were 1 of 96% and 3 of between 76% and 80%. This suggests that arrest of the heart before interruption of the coronary flow for only fifteen minutes at 37°C exerted a little protective action. What was demonstrated clearly was that mere deprivation of coronary flow did not rapidly lead to arrest of the beat, for in all four experiments the hearts beat continuously over the fifteen-minute periods.

Recoveries after 30 Minutes' Arrest of Beat and Occlusion of Coronary Flow at 37°C

10 hearts were used, and the results are given in table II. Of the 5 hearts in the group in which it was the first experiment 2 hearts were also used in the group of 7 in which thirty minutes of arrest took place as the 2nd–8th experiment on each heart. The results are, on the whole, good but suggest that, after this longer period of arrest, hearts stand a better chance of recovering well the first time. Times for the initiation of beat on restoring perfusion with pure Locke's solution varied from thirty seconds to three minutes.

Recoveries after 30 Minutes' Arrest of Beat and Occlusion of Coronary Flow at 25°C

Potassium-citrate arrest was also induced at 25°C in 2 of the hearts in which recovery after arrest at 37°C had been 90% and 81%. Under the conditions of arrest at the lowered temperature rapid rewarming to 37°C and perfusion with pure Locke's solution gave 100% recovery in both cases within ten minutes.

Recoveries after 30 Minutes without Coronary Flow and without Previous Arrest of Beat at 37°C and 25°C

4 hearts were used. It was a notable feature that after interruption of the coronary flow ventricular beats persisted with steadily diminishing force for fifteen to twenty-five minutes.

1 heart had been used in the series arrested by potassium citrate at 37°C for fifteen minutes, and under those conditions its recovery was 100%. In the present series,

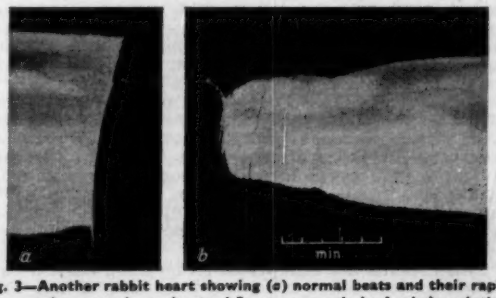

Fig. 3—Another rabbit heart showing (a) normal beats and their rapid arrest by potassium citrate 1·5 mg. per ml. in Locke's solution (coronary flow was occluded for 30 minutes after arrest of the beat) and (b) recovery on restoration of coronary perfusion with pure Locke's solution.

deprived of coronary flow for thirty minutes at 37°C with no previous arrest, it was still able to recover by 76%. The other 3 had all been used in the series of potassium-citrate arrests for thirty minutes at 37°C, when their recoveries were 79%, 78%, and 83% against 22%, 4%, and nil in the present series. In the case of the heart with no ventricular recovery the auricles did recover their beat. 1 heart was deprived of coronary flow twice for thirty minutes at 25°C without previous arrest of the beat, which continued, though diminished, throughout. Its recoveries were then 81% and 94% compared with 100% when arrested by potassium citrate and deprived of coronary flow for 30 minutes at 37° on the first occasion and 90% on a second occasion. From these results on hearts with coronary flow occluded for thirty minutes it appears that previous arrest of the beat is essential for good recovery.

Recoveries after 40 Minutes or more of Arrest of Beat and Occlusion of Coronary Flow at 37°C

8 hearts were used, all of which had been previously arrested by potassium citrate for periods of fifteen or thirty minutes with recoveries of 100% in 3 cases, 93% in 1 case, and 84% in 1. However, after forty-five minutes' arrest by potassium citrate without coronary flow, recoveries were 72%, 20%, and 10% for the 3 hearts used, and after arrests of fifty to eighty-five minutes recoveries were 30–40% for the 3 others. That these poor results were due to the prolonged lack of coronary flow and not to any toxic effect of potassium citrate at 1·0–1·5 mg. per ml. seems likely because, when 4 hearts were perfused continuously for forty minutes to two hours with 1·0–1·5 mg. per ml. of potassium citrate in Locke's solution, their recoveries when returned to pure Locke's solution were all within 70–96%.

These results suggest that, at least for hearts under these experimental conditions, the limit for interruption of coronary flow at 37°C with the beat arrested is probably between thirty and forty-five minutes if good recovery is to be expected.

Continuous Coronary Flow with Potassium Citrate: Effects of Varying Concentration and Duration

10 hearts were used. In 8 of them the effect was observed of potassium citrate at 1, 5, and 10 mg. per ml. perfused for fifteen minutes, and in the 2 others the effects of potassium citrate 1·0 and 1·5 mg. per ml. perfused for 5, 10, 15, 20, 30, and 40 minutes. Recovery periods on pure Locke's solution were of the same duration as the perfusions with potassium citrate.

In every case the distinction was very clear that constant perfusion of any concentration used always led to a much poorer degree of recovery than after an equal period with flow interrupted once that concentration had stopped the heart beating. This was particularly evident with concentrations of 5 mg. per ml. or more. The times elapsing before the first recovery beat, as well as being longer the higher the concentration of potassium citrate used, were also at least doubled when perfusion was continuous.

Varying the duration of perfusion of the least dose necessary to arrest a heart seemed to be less important. In these tests the effects of short perfusions (five minutes) of potassium citrate were always interpolated between perfusions of greater duration. This was to see whether poor recovery as a result of long perfusion had lessened the power of the heart to recover even from an innocuous duration of perfusion causing arrest. Such damage was not seen. Thus, even in the case of a heart perfused for 6 periods of five minutes with 1·5 mg. per ml. of potassium citrate in the Locke's solution, its recoveries were still 100% within fifteen minutes on pure Locke's solution, even after six hours of experiment during which spells of thirty or forty minutes on continuous potassium citrate had resulted in recoveries of 87% and 85% respectively. The times elapsing till the first recovery beats took place lengthened from one and a half minutes to two minutes.

These results are interpreted as meaning that, if controlled cardiac arrest is necessary for such a long time that the heart has to be reoxygenated by a continuous or intermittent closed circuit of coronary perfusion, it would be important to use the lowest concentration of potassium citrate which would arrest the heart.

The Rôle of Potassium and Citrate Ions in causing Cardiac Arrest by Potassium Citrate

11 hearts were used. It was simply demonstrated in each of these hearts that citrate as the sodium salt, at a concentration in the Locke's solution chemically equivalent to that of potassium citrate sufficient to cause cardiac arrest, did little more than reduce the amplitude of contraction by about a half. Recovery was rapid and complete with pure Locke's solution. Even ten times the concentration of sodium citrate did not arrest the beat but reduced it to a barely recordable level. Similarly a chemically equivalent concentration of potassium given as potassium chloride reduced the amplitude of contraction by about two-thirds, and recovery was also rapid and complete on returning to pure Locke's solution. With such concentrations of potassium chloride present, however, two to three minutes of perfusion usually caused ventricular fibrillation. Higher concentrations of potassium chloride by itself caused rapid arrest, but ventricular fibrillation was often seen either at the beginning of the arrest phase or during recovery on pure Locke's solution. From these experiments it seemed obvious that both the potassium and the citrate ions contributed to cardiac arrest by potassium citrate, and that the citrate protected the heart from ventricular fibrillation caused by certain concentrations of the potassium ion. The experiments described below were made to investigate this last point.

Effects of Reduced Concentration of Calcium Ions on Ventricular Fibrillation induced by Potassium Chloride

In 2 of 3 hearts in which potassium chloride produced ventricular fibrillation within three minutes of its perfusion the same concentration of potassium chloride perfused in Locke's solution with only a quarter of the calcium chloride normally present in Locke's solution did not cause fibrillation. Repeating arrest with the same concentration of potassium chloride but in Locke's solution containing the normal concentration of calcium chloride again produced fibrillation. This repetition was important because it was found that potassium chloride would not invariably produce fibrillation each time it was used in a heart in which it had done so once already.

HUMAN FŒTAL HEARTS

4 hearts were used from fœtuses aged 16–20 weeks. The dead fœtuses were not received until more than thirty minutes after removal from the mothers. In every case perfusion with Locke's solution caused good cardiac revival, with regular beats, within twenty minutes. Potassium citrate 1 mg. per ml. rapidly arrested these hearts, and in all 4 hearts revival after fifteen minutes at 37°C without coronary flow reached 100% within five minutes. They were also able under the experimental conditions to recover fully from at least forty-five minutes' deprivation of coronary flow without previous arrest of the beat.

These results were taken to indicate merely that, for the human fœtus, a concentration of potassium citrate sufficient to arrest the heart did not cause lasting damage. No conclusion could be drawn about arrest of the beat improving survival without coronary flow since the resistance of the fœtal heart to asphyxia seemed to be very high in any case.

Discussion

The main bulk of the work was concerned with hearts subjected to fifteen minutes' arrest of beat with potassium citrate and occlusion of coronary flow because it was felt that there were many surgical operations on the heart which could be completed in this time. Thirty minutes' deprivation of coronary flow at 37°C seemed to be about the limit of what might be risked with reasonable hope of good cardiac recovery, but it is likely that hearts in situ can be safely arrested for longer when able to recover with the aid of blood and not merely some saline substitute of limited oxygen-carrying capacity. With arrest of coronary flow for only fifteen minutes recovery was only a little improved by previous arrest of the beat, but for thirty-minute periods previous arrest of the beat greatly improved recovery. It has been shown (Bentall and

Melrose 1957) that lactic acid accumulates in the arrested heart, and that this formation of lactic acid is greater in the beating heart without coronary flow than in the previously arrested heart. The quantity formed during arrest is, however, as much as a third of that formed during anoxia with the heart continuing to beat. From this it may be deduced that the rate of anaerobic respiration of the heart with coronary flow suspended, even when arrested, is still considerable and may be as great as a third of that while beating under similar conditions. It was therefore to be expected that a combination of cooling to 25°C and arrest of the beat would give the best results.

It is probable that, from the point of view of protection of the myocardium, there is no particular virtue in potassium citrate as an arresting agent compared with others, such as potassium chloride. Nor may there be much advantage if only the criteria of a flaccid diastolic arrest with no escape beats are considered; but, when to these is added the question of ventricular fibrillation, it is clear that potassium citrate has much to offer. In the series of experiments with potassium citrate reported here ventricular fibrillation was the exception. It might be argued that it is difficult to induce ventricular fibrillation in the rabbit heart, but certain concentrations of potassium chloride induced it frequently. It is difficult to agree with Kolff et al. (1957), who concluded that the citrate moiety played no useful part in arrest by potassium citrate. The results presented here show that concentrations of potassium chloride, or of sodium citrate chemically equivalent to the lowest concentrations of potassium citrate that would cause arrest, did not arrest the heart, and that concentrations of potassium chloride causing ventricular fibrillation might not do so when the level of calcium in the perfusion fluid was lowered.

It might appear contrary to some experience to state that potassium chloride causes ventricular fibrillation. Burn (1957) drew attention to and much extended observations that potassium chloride can arrest ventricular fibrillation, and Lam et al. (1955) have also given a brief summary of such observations. It is probable that it is all a matter of concentration of potassium chloride, for Lam et al. also recorded that ventricular fibrillation usually took place as a result of using potassium-chloride arrest of the heart, and the concentrations of potassium chloride necessary to achieve cardiac arrest are far higher than those recommended for preventing fibrillation. Since reduced calcium concentration appears to make fibrillation less likely, it is possible that the citrate moiety of potassium citrate, by virtue of forming its poorly ionised calcium salt, protects against any dangerous concentration of potassium ions which result when conditions are changing during the arrival or the washing out of arresting doses of potassium citrate. Excessively high concentrations of potassium citrate might be more likely to cause ventricular fibrillation because calcium citrate is partially dissociated, and so the level of ionised calcium might not be sufficiently lowered to protect against certain concentrations of potassium.

Throughout these studies the closer similarity in behaviour of the rabbit heart than that of the dog to the human heart, expected on a theoretical basis from the histological work of Wearn (1939–40), has been most impressive. This fact must be taken into account especially in coming to conclusions about ventricular fibrillation.

It cannot be contended that perfused-heart preparations in any way afford an absolute measure of myocardial activity, but whatever fraction of myocardial work is being measured it is valid to make deductions about the effect of drugs on a comparative basis—i.e., by comparing the recorded activity during and after the action of a drug with the recorded activity before its action.

From time to time the objection is also raised that hearts subjected to artificial experimental conditions cannot yield results directly applicable to hearts normally in situ. It must certainly be admitted that the hearts now described, existing on an oxygenated modification of Ringer's solution, undoubtedly belong to what has been categorised as "the grossly enfeebled heart of the pharmacological laboratory." But if such hearts can recover well from the action of drugs which arrest them and from the simultaneous effects of total deprivation of coronary flow, the heart in situ, with oxygenated blood, can be expected to do even better, and this has now been borne out by evidence from work on dogs and successful cardiac surgery in man with potassium-citrate arrest.

Summary

Potassium citrate was tested as an arresting agent in 60 rabbit hearts and in 4 human fœtal hearts isolated and perfused with Locke's solution by the well-known Martin-Langendorff technique. Hearts were maintained at a controlled temperature even when arrested and without coronary flow.

Potassium citrate (1–2 mg. per ml.) arrested all hearts in ten to thirty seconds. The myocardium remained completely flaccid, without fibrillation, and without escape beats. Hearts in this state, deprived of all coronary flow for thirty minutes at 37°C, recovered well after the restoration of coronary perfusion with pure Locke's solution. No stimulant or other antidote was required. Recovery was maximal in five to fifteen minutes. These results are compared with those obtained by simple occlusion of the coronary flow.

The rôles of the potassium and the citrate ions are discussed. Evidence is presented that potassium citrate is more effective and less likely to provoke ventricular fibrillation than are equivalent concentrations of potassium chloride.

We are greatly indebted to Miss Jean Phillips for technical assistance.

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THE VALUE OF RENAL BIOPSY

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RENAL biopsy is now accepted as a practical method of investigation. Its use in research is recognised, but in ordinary clinical practice its value remains debatable. Iversen and Brun (1951), Kark and Muehrcke (1954), and Muehrcke et al. (1955a) have shown that the renal biopsy technique can be both successful and relatively safe; already over 1000 biopsies have been reported (Muehrcke et al. 1956). In this country the technique has received slow recognition and is still regarded as somewhat dangerous, giving information of value to the pathologist but being of little help to the patient. In addition there is a natural tendency to regard the claims of the originators as over-enthusiastic.

We record here our experience with renal biopsy in 26 patients and assess its diagnostic and prognostic value from the clinical point of view.

Technique

The technique used has been described by Kark and Muehrcke (1954) and Muehrcke et al. (1955a) using the modified Vim-Silverman needle.

The full technique will not be described, but certain aspects require special attention. Premedication should produce a relaxed and coöperative patient, inadequate dosage producing apprehension and restlessness. We now give to an adult quinalbarbitone gr. 3 an hour before, and intramuscular pethidine 100 mg. half an hour before, the biopsy. This dosage has not led to any loss of coöperation. A rolled blanket placed under the upper abdomen is as effective as, and more comfortable than, a sandbag. The location of underlying bony prominences, in particular the iliac crest, may be difficult in fat, muscular, or œdematous patients, but the vertebral spines and twelfth rib are usually easily felt. There may therefore be some doubt about the longitudinal measurement from the iliac crest; but, providing the biopsy is made $^1/_2$–1 inch below the last rib, no difficulty arises. Error in the lateral measurement from the spine is unlikely. It is very important to establish that the needle is in the kidney; the needle can be felt to enter a firm kidney but not a soft (œdematous) one and may pulsate when in the kidney. More reliable evidence, however, is the characteristic swing of the needle on respiration. In some patients this swing was not obtained, since in the prone position their respiratory movements were entirely costal; but instructions to breathe with the diaphragm immediately established the characteristic swing. The actual taking of the biopsy specimen is the most difficult part of the procedure, and success can only be achieved by practice.

Biopsy was done successfully on 25 occasions in 26 patients. There was complete failure in 1 case, and inadequate specimens were obtained in 2 others. Tissue was obtained from right and left kidneys with equal ease. Both of us found difficulty in some patients with the nephrotic syndrome. Although we were certain that the needle was in the kidney, no adequate specimen was obtained, and it was necessary to introduce the needle again; we suspect that the soft œdematous kidney was not gripped by the needle. In the one complete failure obesity, œdema, and a scoliosis made the operation difficult.

Complications

Complications were infrequent. Backache, renal colic, retroperitoneal hæmatoma, and hæmaturia were encountered. Pain in the loin was recorded in 6 patients, but in most it was only a mild local soreness which cleared up in twenty-four hours. 2 patients developed more severe local back pain requiring minor analgesics and persisting for one to three days; in 1 patient this was accompanied by vomiting. We suspect that these symptoms were due to a small hæmatoma. 1 patient developed renal colic nine hours after the biopsy; this rapidly settled but recurred for a short time forty-eight hours later.

1 patient developed a large retroperitoneal hæmatoma which necessitated blood-transfusion. He had malignant hypertension (blood-pressure 240/160 mm. Hg) with uræmia (blood-urea 96 mg. per 100 ml.) and had had chronic osteomyelitis for many years. A Congo-red test was negative. The biopsy specimen from his right kidney showed severe amyloid infiltration of the glomeruli and blood-vessels, including a large artery from which the bleeding had probably occurred. There was no hæmaturia. Fourteen days after the biopsy the patient left hospital symptom-free. There had been no obvious contra-indication to biopsy. Intravenous pyelography had been impossible because of his poor renal function, but straight radiography of his abdomen showed the renal outlines clearly and was used for measurements.

5 patients had visible hæmaturia but never longer than for twenty-four hours. 2 other patients had transient hæmaturia demonstrable by the guaiacum test. The significance of a few red cells in the centrifuged and uncentrifuged urinary deposits was difficult to assess when pre-existing microscopic hæmaturia had been present. On several occasions the specimens showed that arteries up to the size of arcuates had been cut, but there was no correlation between this finding and observed hæmaturia or backache.

Some patients did not pass urine for up to six hours after the operation in spite of drinking large quantities of water. Apparently this was not due to bladder retention but was thought to be a minor suppression of urine associated with the premedication.

1 patient died three months after biopsy, and at necropsy the needle marks could just be identified with the naked eye as minute spots on the cortex of the kidney.

We have accepted the contra-indications stated by Kark and Muehrcke (1954); so that we have not performed biopsies in the presence of any hæmorrhagic tendency, suspected cystic kidneys, hydronephrosis, or neoplasm; nor have we done a biopsy on an only kidney. No patient was uncoöperative.

Interpretation of Histological Findings

The interpretation of histological changes in the kidney is traditionally difficult, even when there is no limitation on the amount of tissue available. It is therefore self-evident that the changes in a needle biopsy specimen containing only few glomeruli may be extremely difficult or even impossible to interpret even by those conversant with the pathological histology of the kidney. All our specimens contained both cortex and medulla and measured 5–20 mm. in length. In the sections of our 25 biopsy specimens there were 10–36 glomeruli in 20 and less than 10 in the remaining 5. These latter were usually from contracted kidneys. In all our hypertensive patients sections of arteries and arterioles were present, and often arcuate arteries were seen.

In diffuse renal disease the tissue obtained is obviously representative of the rest of the kidney. In conditions where the renal lesions are focal—e.g., pyelonephritis and early malignant essential hypertension—it is possible for the diagnosis to be missed; but in our small series we have so far been able to make a histological diagnosis in such cases.

Distortion of the microscopic structure was slight, probably because this method does not involve drilling. The histological detail was excellent, and tubular epithelium in particular was better preserved than in necropsy material, which is subject to autolysis. Fibrinoid material in arteriolar necrosis does not take the hæmatoxylin and eosin stain in biopsy tissue as well as in necropsy specimens; we had previously noticed this difference in renal biopsy material taken during thoracolumbar sympathectomy for hypertension. Sections stained with hæmatoxylin and eosin and by the van Gieson, periodic-acid/Schiff, and Heidenhain's azan methods have been sufficient for most purposes; Congo-red and methyl-violet have been used to confirm the presence of amyloid.

Histological diagnosis has been made with ease and certainty in the following conditions: amyloid disease; benign essential hypertension; malignant essential hypertension (on the finding of arteriolar necrosis or of endarteritis fibrosa of the interlobular arteries); and type-II nephritis (on the finding of thickened basement membrane or of intercapillary hyalinisation).

Chronic type-I nephritis and chronic pyelonephritis have in some instances been easy to identify, but in others, in which there was severe renal contraction with ischæmic loss of glomeruli, the differentiation was difficult.

The histological findings in 13 cases of the nephrotic syndrome were of particular interest. 2 patients were found to have amyloid disease; in 6 others the charac-

teristic changes of type-II nephritis were present. In the remaining 5 cases histological lesions were scanty; in the glomeruli no thickening of the basement membrane and no intercapillary hyalinisation were found, but slight increase in the cellularity of the glomerular tuft, capsular adhesions, and "bland" focal lesions of the tuft were seen. In such cases we attach little diagnostic importance to tubular changes such as slight flattening of the epithelium, dilatation of the lumen, and albuminous or lipoid inclusions. We regard the histological changes in these 5 cases as evidence of early type-II nephritis because these patients in their clinical course, so far as it had been followed, closely resembled other patients in whom the diagnosis of type-II nephritis was proved subsequently at necropsy. This is in accordance with the Ellis (1942) classification. The diagnosis type-II nephritis is preferable to the label nephrotic syndrome because it indicates a disease with a well-documented natural history and prognosis (Ellis 1942). With histological changes so inconspicuous there is no anatomical counterpart of the functional lesion which is responsible for the gross proteinuria. We have not yet done biopsies on patients with the nephrotic syndrome due to renal-vein thrombosis, diabetic glomerulosclerosis, systemic lupus erythematosus, or of rapidly progressive type-I nephritis.

Illustrative Case-reports

We have used renal biopsy in an attempt to solve some of the more difficult problems which arise in the diagnosis and management of patients with renal disease. The value of the procedure in patients with hypertension, suspected amyloid disease, the nephrotic syndrome, and unusual forms of nephritis will be discussed. The cases cited are those in which renal biopsy was the most informative; in the remainder the results had no definite value other than for confirmation of either diagnosis or prognosis.

Hypertension

The usual clinical, laboratory, and radiological investigations do not always reveal the ætiology of hypertension. This is no longer a matter of merely academic interest now that effective therapy is available. The following case-reports illustrate the value of biopsy findings in the management of the patients:

Case 1.—A man, aged 37, was admitted in June, 1956, with six weeks' history of severe headaches and four days' history of blurring of vision.

On examination he had blood-pressure 260/175 mm. Hg and severe papilloedema with retinal hæmorrhages and exudates. His urine boiled "solid" with protein; there were no casts in the deposit. He had blood-urea 39 mg. per 100 ml., maximal urine urea concentration 1·62 g. per 100 ml.; and normal intravenous pyelograms.

Diagnosis.—Malignant essential hypertension was the presumptive diagnosis, but the gross proteinuria suggested nephritis.

Biopsy of the right kidney showed no evidence of nephritis but considerable arteriolar damage with fibrinoid necrosis. This confirmed the diagnosis of malignant essential hypertension, and treatment with hypotensive drugs was pursued more intensively than might have been thought justifiable in a case of nephritis.

Case 2.—A man, aged 48, complained of recurrent pain in his right loin and of hæmaturia in 1956. Hypertension had been recorded fourteen years earlier.

On admission he had blood-pressure 215/140 mm. Hg and retinal hæmorrhages but no exudates or papilloedema. He had slight proteinuria; no acid-fast bacilli in urine; blood-urea 30 mg. per 100 ml.; maximal urine urea concentration 2·04 g. per 100 ml.; normal intravenous pyelograms and a normal right ureterogram. Cystoscopy on one occasion showed small vesical submucous hæmorrhages.

Diagnosis.—This lay between severe benign hypertension with focal vascular damage leading to hæmaturia and proteinuria, and chronic nephritis.

Biopsy of the left kidney showed no evidence of glomerulonephritis. There was focal fibrosis with tubular degeneration and glomerular hyalinisation. The arterioles showed medial hypertrophy and hyalinisation, and the larger vessels showed medial hypertrophy and degenerative changes.

In view of the severe arteriolar changes the diagnosis of severe essential hypertension with recurrent hæmaturia was confirmed. The patient has since developed papilloedema and is being treated with hypotensive drugs.

The differentiation between papilloedema due to malignant hypertension and papilloedema due to an intracranial tumour with coincidental benign essential hypertension may be difficult (Jefferson 1955). Renal biopsy may reveal the characteristic lesions of malignant hypertension:

Case 3.—A woman, aged 53, had a left perirenal abscess drained in 1950. In 1952 she had further treatment for a similar complaint. In 1956, after a week of drowsiness, she vomited and became unconscious. She recovered consciousness after several days but remained drowsy and confused.

On examination she had blood-pressure 240/130 mm. Hg, bilateral gross papilloedema and retinal hæmorrhages and exudates; slight expressive aphasia; right facial weakness; weakness of the right upper limb; slight proteinuria in three of fifteen specimens of urine; and blood-urea 41 mg. per 100 ml. Renal-function tests were unsatisfactory owing to lack of coöperation. Intravenous pyelograms were normal.

Diagnosis.—A clinical diagnosis of a cerebral neoplasm with coincidental hypertension was made, but electro-encephalography, left cerebral angiography, ventriculography, and brain smears revealed no definite abnormality.

Biopsy of the right kidney showed severe arteriolar changes, with endarteritis fibrosa and slight focal interstitial fibrosis. The final diagnosis was malignant hypertension, probably essential in origin, but chronic pyelonephritis could not be excluded.

The difficulty of assessing the benefit to be obtained from nephrectomy in suspected unilateral renal disease with hypertension is well recognised (Pickering and Heptinstall 1953, Graber and Shackman 1956). A knowledge of possible structural damage in the opposite kidney is of importance. This may be either primary renal disease—e.g., chronic pyelonephritis—or secondary to the hypertension, and its severity is one indication of the relief of hypertension which may follow nephrectomy. There is, of course, a slight risk in taking a biopsy specimen from the apparently normal kidney, because any severe damage might aggravate the hypertension. The following case illustrates the problem:

Case 4.—A woman, aged 34, complained in November, 1956, of blurred vision and early morning headaches.

She had no past history of renal disease.

On admission she had blood-pressure 270/150 mm. Hg; retinal hæmorrhages and exudates but no papilloedema. Her urine contained a trace of protein and on culture proved sterile. She had blood-urea 27 mg. per 100 ml.; and maximal urine urea concentration 2·76 g. per 100 ml. Intravenous pyelograms and presacral oxygen insufflation revealed a small right kidney and a left kidney of normal size. A left ureteric specimen of urine contained protein and a few leucocytes. Right nephrectomy was considered, but in view of the protein in the left ureteric specimen it was felt that damage to the left kidney might be sufficient to maintain the hypertension.

Biopsy of the left kidney showed severe medial hypertrophy and subintimal hyalinisation in the arterioles and hypertensive glomerular lesions. There were also areas of interstitial fibrosis, dilated tubules, and slight chronic inflammatory infiltration. These changes were considered to indicate chronic pyelonephritis and hypertensive damage in the left kidney and to contra-indicate right nephrectomy. The patient was therefore treated medically.

Amyloid Disease

Amyloid disease may be revealed unexpectedly in a patient with the nephrotic syndrome and probably indicates a worse prognosis than the finding of type-II nephritis:

Case 5.—A woman, aged 54, had had chorea and rheumatic fever at the age of 7 years. In 1952 she had recurrent swelling of ankles; at that time mitral stenosis was found, with slight œdema, heavy proteinuria, low plasma-protein levels, normal

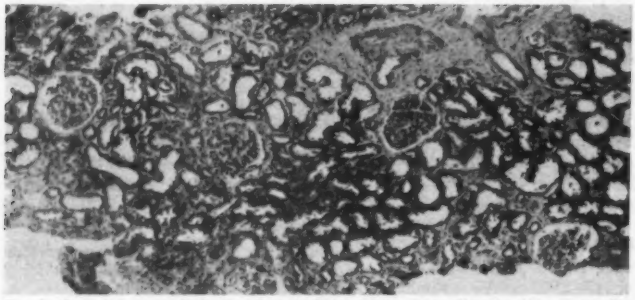

Fig. 1—Case 8: normal glomeruli and slight perivascular fibrosis. (Hæmatoxylin and eosin. ×60.)

blood-pressure, and normal renal-function tests. Type-II nephritis and rheumatic carditis were diagnosed. She was treated with a high-protein diet and mercurial diuretics, with fair control of the œdema. In 1956 she was admitted because of increased œdema and a fall in the plasma-albumin level.

Biopsy of the left kidney disclosed amyloid disease. No evidence of the disease was found elsewhere, nor was there any evidence of chronic pyogenic infection.

On the other hand, the nephrotic syndrome in a patient with long-standing infection may not be due to amyloid disease:

Case 6.—A man, aged 62, had twenty-one years' history of cough, with copious, purulent, and occasionally bloodstained sputum, and five months' history of increasing œdema, which was treated with high-protein diet, diuretics, ion-exchange resins, and cortisone. In January, 1956, he had moderate œdema of the legs and sacrum.

On examination he had blood-pressure 150/80 mm. Hg; persistent crepitations at the base of his right lung; heavy proteinuria; blood-urea 102 mg. per 100 ml., maximal urine urea concentration 1·2 g. per 100 ml., plasma-proteins 4·5 g. per 100 ml. (albumin 2·2 g., globulin 2·3 g.). Radiography showed increased right basal markings in his chest and normal renal outlines. Congo-red test within normal limits.

Diagnosis.—Amyloid disease with chronic bronchiectasis was considered to be likely.

Biopsy of his right kidney showed focal necroses and intercapillary hyalinisation in the glomeruli, with capsular adhesions and interstitial fibrosis. There was no evidence of amyloid disease. The final diagnosis was type-II nephritis running a fairly rapid course with renal failure but with only slight hypertension. The patient died in uræmia four months after the biopsy. There was no necropsy.

Amyloid disease was disclosed unexpectedly in the 1 patient in whom renal biopsy failed:

Case 7.—A man, aged 41, had several years' history of lumbar backache radiating to his buttocks, and nine months' history of œdema and increased frequency of micturition. He had lost 2 stone in weight.

Fig. 3—Case 10: glomerulus showing thickening of basement membrane of capillaries and intercapillary hyalinisation. (Heidenhain's azan. ×230.)

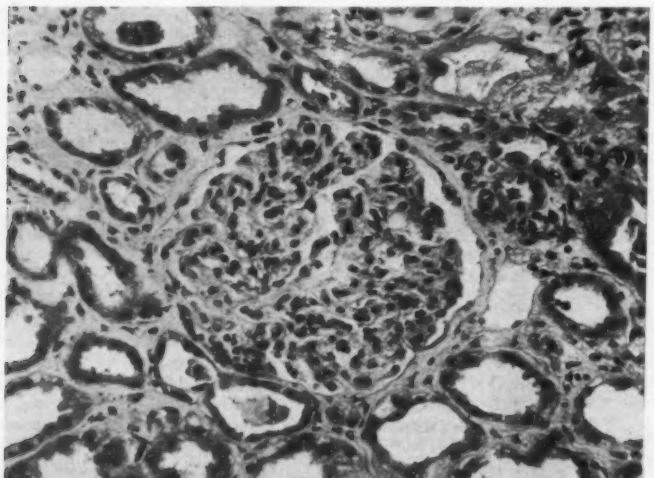

Fig. 2—Case 9: glomerulus showing slight increase in cellularity and capsular adhesions. (Hæmatoxylin and eosin. ×250.)

On examination he was obese and had slight œdema; blood-pressure 150/90 mm. Hg; no enlargement of liver or spleen and no joint abnormality; moderate lumbar scoliosis; slight proteinuria; a few red and white cells in his urine; blood-urea 25 mg. per 100 ml.; and plasma-proteins 6·0 g. per 100 ml. (albumin 2·9 g., globulin 3·1 g.).

Biopsy.—The right renal outline was poorly demonstrated by intravenous pyelography; so the left kidney was chosen for biopsy. The procedure was apparently done without complication, but only small fragments of tissue were obtained. These proved to be from the spleen, which showed diffuse amyloid infiltration.

Nephrotic Syndrome

As has been pointed out above, all our cases of nephrotic syndrome proved, in our opinion, to be examples of either type-II nephritis or amyloid disease. We have therefore no experience of other causes of the syndrome being revealed unexpectedly by biopsy. In our view the diagnosis of type-II nephritis can usually be made on clinical evidence by exclusion of the other causes of the nephrotic syndrome. Renal biopsy serves further to exclude some of

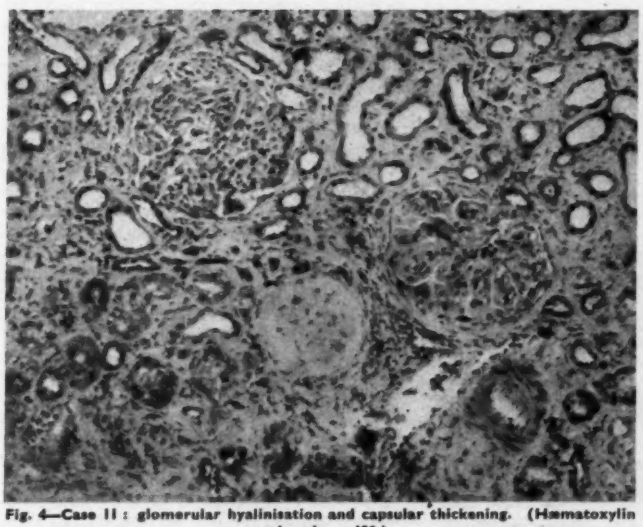

Fig. 4—Case 11: glomerular hyalinisation and capsular thickening. (Hæmatoxylin and eosin. ×120.)

these other causes. However, in early cases histological changes in type-II nephritis may be very inconspicuous. Scanty glomerular lesions without diffuse thickening of the basement membrane or intercapillary hyalinisation indicate an early stage of the disease from which the patient may recover spontaneously or after therapy. Case-reports have been chosen to illustrate four stages of renal damage in type-II nephritis:

Case 8.—A woman, aged 40, is believed to have had nephritis following scarlet fever in 1923. In 1944 and 1947 her urine was normal. In March, 1956, she noticed undue frothiness of her urine and a week later swelling of her ankles.

On examination she had slight ankle and sacral œdema; blood-pressure 100/80 mm. Hg; 24-hour protein loss up to 35 g.; renal-function tests normal; plasma-proteins 4·0 g. per 100 ml. (albumin 1·4 g., globulin 2·6 g.); blood-cholesterol 210 mg. per 100 ml.; and intravenous pyelograms normal.

Diagnosis.—She was considered to have type-II nephritis, but her past history suggested the possibility of an attack of type-I nephritis.

Treatment with prednisone in June, 1956, was accompanied by a massive diuresis; she became free from œdema and proteinuria and her plasma-protein levels returned to normal.

Biopsy.—A section from her right kidney before treatment was started contained thirteen glomeruli. There was a capsular adhesion in one glomerulus but no definite thickening of the basement membrane or intercapillary hyalinisation. There was patchy perivascular cellular interstitial fibrosis (fig. 1). This was considered to be an example of early type-II nephritis with minimal histological changes. It is in such cases that recovery might be expected.

Case 9.—A man, aged 35, developed œdema in February, 1956, and was found to have heavy proteinuria with low plasma-protein levels. In June, 1956, he was admitted with slight œdema, blood-pressure 150/100 mm. Hg, daily urinary protein loss up to 27 g., plasma-proteins 5·9 g. per 100 ml. (albumin 2·9 g., globulin 3·0 g.), and blood-urea 45 mg. per 100 ml.

Biopsy.—An attempt at right renal biopsy failed, but a successful left renal biopsy showed slight proliferative glomerulitis and occasional adhesions between glomerular tufts and capsules (fig. 2). There was no thickening of the basement membrane or intercapillary hyalinisation in the glomeruli. There was very slight cellular interstitial fibrosis.

Course.—While under treatment with prednisone the patient had a massive diuresis, but later he again became œdematous, and he died with rapidly spreading cellulitis (Ross and Ross 1957). Histological examination of the kidneys post mortem showed an exactly similar picture to that described above.

Case 10.—A man, aged 58, developed œdema and heavy proteinuria in February, 1956. He was admitted in October with slight œdema but no other physical abnormality.

On examination he had blood-pressure 135/85 mm. Hg; daily urinary protein loss up to 19 g.; blood-urea 36 mg. per 100 ml.; maximal urine urea concentration 2·52 g. per 100 ml.; intravenous pyelograms normal; plasma-proteins 5·1 g. per 100 ml. (albumin 2·2 g., globulin 2·9 g.).

Biopsy of his left kidney showed type-II nephritis with thickening of the basement membrane and intercapillary hyalinisation, confirming the clinical diagnosis (fig. 3).

Treatment.—It was thought unlikely that steroid therapy would be successful in view of the renal changes. Two months' treatment with prednisone did not produce a diuresis and mercurial diuretics and acupuncture were used to reduce his œdema.

Case 11.—A man, aged 21, first noticed œdema in June, 1955, about a month after a sore throat. The œdema increased but later responded to treatment with high-protein low-salt diet, there being no œdema in January, 1956.

On examination he had blood-pressure up to 200/120 mm. Hg; no retinopathy; heavy proteinuria; urine positive to guaiacum test and containing granular casts in deposit; blood-urea 45 mg. per 100 ml.; maximal urine concentration 1·44 g. per 100 ml.; intravenous pyelograms normal; plasma-proteins 4·8 g. per 100 ml. (albumin 2·4 g., globulin 2·4 g.).

Diagnosis.—Clinically the patient was considered to have type-II nephritis in which the nephrotic syndrome had been followed by progressive renal impairment with rising blood-pressure. Type-I nephritis running a rapidly progressive course was considered possible but unlikely in the absence of frank hæmaturia initially and the insidious onset of œdema associated with heavy proteinuria.

Biopsy of the right kidney showed advanced type-II nephritis with proliferative glomerulitis, thickening of the basement membrane, and various stages of glomerular hyalinisation (fig. 4).

Nephritis of Unusual Type

Two case-reports illustrate the diagnostic value of renal biopsy when the clinical evidence is uncertain. It

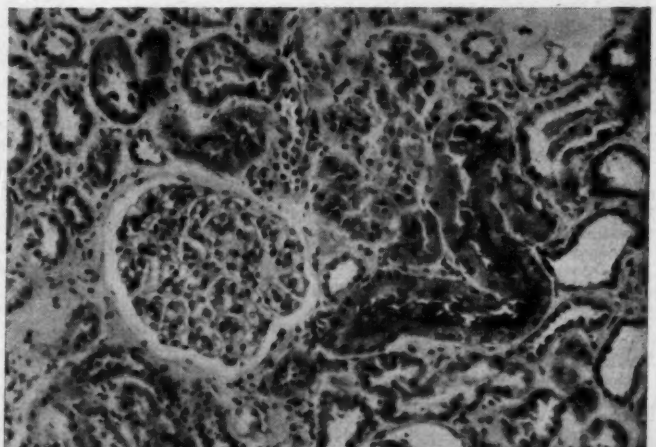

Fig. 5—Case 13: normal glomerulus, and blood in convoluted tubule. (Hæmatoxylin and eosin. ×175.)

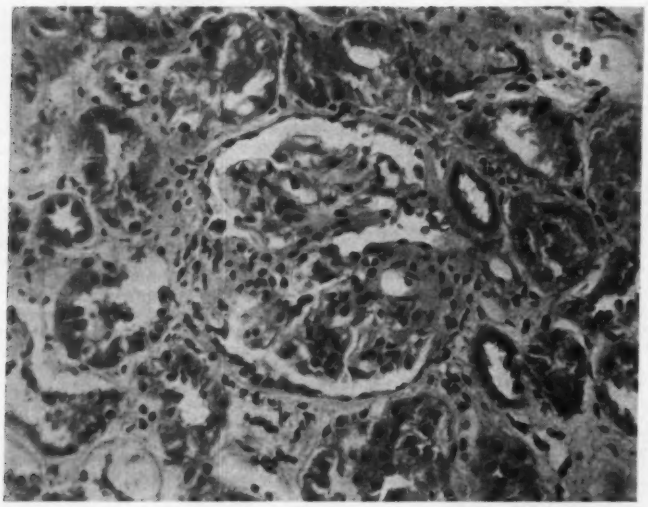

Fig. 6—Case 13: glomerulus showing focal lesion with capsular adhesions. (Hæmatoxylin and eosin. ×260.)

cannot, however, be claimed that the findings had any great influence on the management of the patients:

Case 12.—A man, aged 47, had six weeks' history of general malaise and intermittent lumbar backache radiating to his loins and three weeks' history of recurrent conjunctivitis (fæcal streptococci cultured). No hæmaturia or œdema.

On examination he had slight pallor; blood-pressure 180/90 mm. Hg; slight proteinuria; a few red and white cells and granular casts in his urine; blood-urea 45 mg. per 100 ml.; maximal urine urea concentration 1·56 g. per 100 ml.; plasma-proteins 7·8 g. per 100 ml. (albumin 3·6 g., globulin 4·2 g.); intravenous pyelograms normal.

Diagnosis.—Clinically this case was rather obscure, but the most likely diagnosis appeared to be progressive type-I nephritis with no history of an acute attack.

Biopsy of the right kidney showed glomerular lesions with focal increase of endothelial cells and slight thickening of the basement membranes (thirty-six glomeruli in section). These changes were thought to be an early stage of type-II nephritis or associated with resolution from an acute attack of nephritis.

Prognosis.—Recovery was thought to be unlikely in view of the structural changes. However, four months after the biopsy the urine was protein-free, blood-pressure 105/70 mm. Hg, plasma-proteins 7·3 g. per 100 ml. (albumin 4·6 g., globulin 2·7 g.), and blood-urea 36 mg. per 100 ml.

Case 13.—A boy, aged 20, had three years' history of recurrent hæmaturia associated with infections of his upper respiratory tract but no œdema or hypertension. Slight proteinuria persisted between these episodes.

On admission he had blood-pressure 125/75 mm. Hg; moderate proteinuria; many red cells and occasional granular casts in his urine; blood-urea 38 mg. per 100 ml.; maximal urine urea concentration 2·0 g. per 100 ml.; plasma-proteins 5·9 g. per 100 ml. (albumin 4·1 g., globulin 1·8 g.); intravenous pyelograms and cystoscopy normal.

Diagnosis.—Recurrent focal nephritis with persistent proteinuria.

Biopsy.—A section from the right kidney contained thirteen glomeruli. Many of these had focal lesions with proliferation of endothelial cells and capsular adhesions. Some of the tubules contained red cells, and there was a slight increase in interstitial tissue (figs. 5 and 6). This histological picture appears to be distinct from that of type-I nephritis and is compatible with the clinical diagnosis of recurrent focal nephritis. We have not found descriptions of similar cases in which the clinical and histological features are correlated.

Discussion

On the basis of these results we are of the opinion that, in expert hands, renal biopsy is safe and practical, but its potential dangers make it unsuitable for general use. Its value may be discussed, on the one hand, in relation to the investigation of the natural history of renal disease and, on the other, as a useful diagnostic procedure in the individual patient.

Renal biopsy has been of undoubted value in the study of the early histological changes in various renal diseases, including diabetic nephropathy (Brun et al. 1953), calcinosis (Bjørneboe et al. 1952), myelomatosis (Greenwald et al. 1953), disseminated lupus erythematosus (Muehrcke et al. 1955b), pyelonephritis (Jackson et al. 1955, Kipnis et al. 1955), anuria (Gormsen et al. 1955), and toxæmia of pregnancy (Pollak et al. 1956). It is of particular interest in the study of those renal diseases from which recovery is possible—e.g., the nephrotic syndrome and focal nephritis.

We consider that some of the claims made for renal biopsy as a diagnostic procedure have been over-enthusiastic. Its value in diagnosis is not always certain, and its usefulness in relation to treatment and prognosis is not always well substantiated. With careful clinical assessment, aided by laboratory and radiological investigations, the correct diagnosis can be made in the great majority of cases of glomerulonephritis. Even in the absence of an exact diagnosis glomerulonephritis can be adequately treated and a reasonable view of the prognosis formed. In most patients in our series the renal-biopsy findings did not alter, but only served to strengthen, previous views on treatment and prognosis. There are, however, some cases in which biopsy can be of definite value, and it is these we wish to emphasise. The chance of biopsy revealing an unexpected diagnosis is small and is perhaps more likely in patients with the nephrotic syndrome. It happened in only 1 of our cases (case 5). With inadequate clinical assessment biopsy will, of course, more frequently provide unexpected diagnoses.

In type-II nephritis there is now considerable evidence that, in some cases, particularly those without hypertension, structural lesions of the glomerulus may be very slight at the onset. The demonstration of this by biopsy does not necessarily indicate that the patient will be one of the fortunate minority who will recover. However, if the changes in the kidney are only slight, recovery will be more likely than if they are severe. We hoped that renal-biopsy findings in early type-II nephritis might indicate the likelihood of a successful therapeutic response to adrenal steroids. Our results so far suggest that successful treatment with prednisone is most likely when glomerular damage is minimal. Such information is of considerable value because renal-function tests are almost always normal and give little indication of the degree of structural glomerular damage. When renal function is impaired, the likelihood of remission, by any means at present available, is negligible.

In hypertensive patients renal biopsy may be of value in the few cases where the ætiology is uncertain, but it must be realised that biopsy cannot entirely exclude such conditions as chronic pyelonephritis and malignant essential hypertension. It can usually exclude or confirm the presence of chronic nephritis as the cause of hypertension. Renal biopsy may be of particular value in patients with unilateral renal disease and hypertension. A renal biopsy on the opposite side will indicate the degree of vascular damage already present and may in addition reveal that the primary renal disease is bilateral. These findings are of importance in assessing the relief of hypertension which may follow nephrectomy. The risk of damaging the opposite kidney during biopsy is

probably more than compensated by the fact that the information provided may prevent the removal of a functioning kidney without relief of the hypertension.

Renal amyloidosis is not common but has to be considered in the presence of a chronic infection. We believe that renal biopsy is the only satisfactory method of confirming or excluding amyloid disease of the kidney.

In a few cases where renal biopsy is used a definite diagnosis cannot be made from a study of the histology alone. This is particularly true in some early cases of nephritis and in the later stages when there are severe hypertensive and ischæmic changes. The lesions of nephritis are not invariably pathognomonic of a particular variety of the disease but are rather an expression of the intensity and duration of the pathological process, including secondary ischæmic changes. In renal disease similar clinical syndromes may result from a variety of pathological lesions; conversely, similar lesions may give rise to a variety of clinical manifestations. It is therefore evident that an accurate diagnosis cannot always be made on clinical grounds or on pathological evidence alone but that both must be studied.

We emphasise that whatever information is revealed by renal biopsy in no way detracts from the necessity for a full and complete clinical investigation. Renal biopsy has an undoubted value in the investigation of the natural history of renal disease, but at present its use in clinical practice should be restricted to carefully selected cases such as we have described.

Summary

The results of renal biopsy in 26 patients are described. The technique used was found to be relatively simple, and complications were rare. The tissue obtained was satisfactory for histological study in most cases.

Renal biopsy is of considerable service in the investigation of renal disease, but its contribution to diagnosis, prognosis, and treatment is of limited value.

We wish to thank Prof. Clifford Wilson and Lord Evans for help in preparing this paper; Dr. R. C. Muehrcke for demonstrating his biopsy technique to us; Prof. Dorothy Russell for allowing us to use sections prepared in the Bernhard Baron Institute of Pathology; and the physicians of the London Hospital for allowing us to do renal biopsies on their patients.

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". . . There is, beyond all dispute, a widespread rejection in the country of religious and therefore denominational interpretations of marriage and divorce, and legal rules based on them no longer command general respect. Despite this, marriage has not lost its hold as a secular institution. Indeed, the new democratic family unit of the mid-twentieth century exhibits a far healthier vitality than its Victorian counterpart. . . . It is of outstanding importance that, in this field, the rule of law should be understood, respected and reasonable. The present system with its accumulating dishonesties and perjuries is damaging to the law and hence detrimental to public morality."—O. R. McGREGOR, *Divorce in England*. London: Heinemann, 1957; p. 195.

SEX DIAGNOSIS BY THE NUCLEAR STRUCTURE OF THE CELLS OF HUMAN URINARY SEDIMENT

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THE presence of sex chromatin in the nuclei of somatic cells was reported by Barr and Bertram (1949) and Moore and Barr (1953).

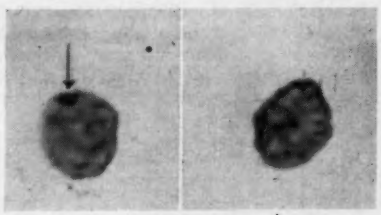
We have looked for sex chromatin (which we have also called "chromoleme") not only in the tissues of different animals but also in normal and pathological human material (Castro and Sasso 1953, Decourt et al. 1954, Castro 1955), and recently have shown that the sex of rats can be determined from the appearance of the ameloblasts in the dental germ (Castro et al. 1956).

In man the sex has been diagnosed from skin-biopsy specimens (Moore et al. 1953), blood smears (Davidson and Smith 1954), smears from oral mucosa (Moore and Barr 1955, Marberger et al. 1955), and sediment from amniotic fluid (Makowski et al. 1956, Sachs et al. 1956).

We report here the possibility of diagnosing sex from urinary sediment.

The material was obtained from 22 women and 28 men, between 20 and 30 years of age, in perfect health so far as we could judge.

The method consists in repeatedly washing, with human serum, the sediment obtained by centrifuging 20 ml. of urine. (On the average, it is washed three times.) With a small cotton-tipped glass rod smears are prepared and rapidly air-dried. The smears are fixed in a mixture of equal parts of ethanol and ether for 2–24 hours, stained with 1% cresyl violet with heat, differentiated in 95% ethanol, cleared in xylol, and mounted in Canada balsam.



a *b*

Epithelial nuclei, stained with cresyl violet, in smears from urinary sediment: *a*, female; *b*, male (×2500).

The results were 100% correct. Females were identified by the presence of sex chromatin in well-preserved cells, seen as a compact mass always adhering to the nuclear membrane and flattened at the point of contact.

For greater accuracy in the diagnosis one must consider as female the smears in which the proportion of cells with sex chromatin is at least 5% of the observed cells, and as males those in which it is less than 5%.

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EFFECT OF LONG-CHAIN POLYUNSATURATED AND SATURATED FATTY ACIDS ON THE SERUM-LIPIDS OF MAN

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MANY investigators have shown that the blood-lipids respond to qualitative alterations in the intake of fats and oils (Kinsell et al. 1953, 1954, 1955, Ahrens et al. 1954, 1957, Beveridge et al. 1955, 1956a and b, Bronte-Stewart et al. 1956, Gopalan and Ramanathan 1956, Malmros and Wigand 1957). In general, they agree that animal fats (such as butter fat, beef dripping, lard, and chicken fat) raise the serum-cholesterol, whereas vegetable fats (such as corn oil, safflower oil, and sesame oil) lower it. Bronte-Stewart et al. (1956) and Malmros and Wigand (1957) showed that marine oils too can lower the serum-cholesterol.

Kinsell and Michaels (1955), Beveridge et al. (1956a), and Bronte-Stewart et al. (1956) attributed the lowering of serum-cholesterol to the long-chain polyunsaturated fatty acids which are abundant in vegetable and marine oils. The action of butter fat in raising the serum-cholesterol has been attributed by Beveridge et al. (1956b) to a volatile fraction of the butter oils.

There has been no uniformity of method in the studies reported. Some investigators have used synthetic diets (Kinsell et al. 1953, 1954, 1955, Ahrens et al. 1954, 1957, Beveridge et al. 1955, 1956a and b, Malmros and Wigand 1957), while others have used a base of natural or "mixed" diet to which various fats and oils have been added (Bronte-Stewart et al. 1956, Gopalan and Ramanathan 1956). Bronte-Stewart et al. studied Bantus, Gopalan and Ramanathan studied Indians, and Kinsell et al., Beveridge et al., and Ahrens et al. studied white North Americans. But, despite the diversity of diets and races studied, there has been agreement in the results reported to date.

The present work compares the effects of corn oil, safflower oil, butter fat, and an ethyl-linoleate concentrate (containing 90% ethyl linoleate, 5% ethyl stearate, and 5% ethyl oleate) obtained from safflower oil, and ethyl stearate.

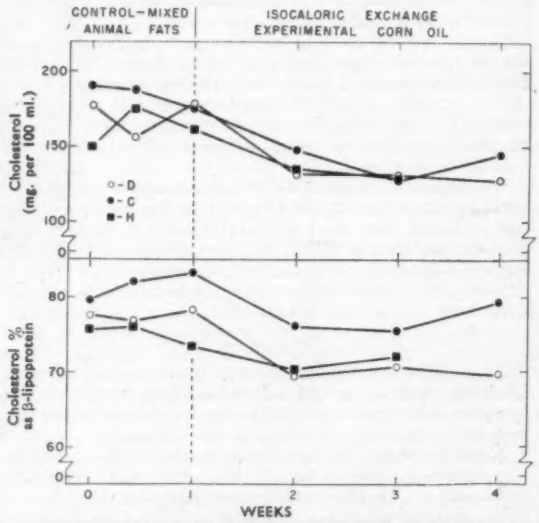

Fig. 1—Experiment 1: isocaloric exchange of corn oil (at 40% of calories) for the mixed fats of the diet. The upper panel shows the change in serum-cholesterol levels, and the lower panel the change in percentage of total serum-cholesterol transported as β-lipoprotein.

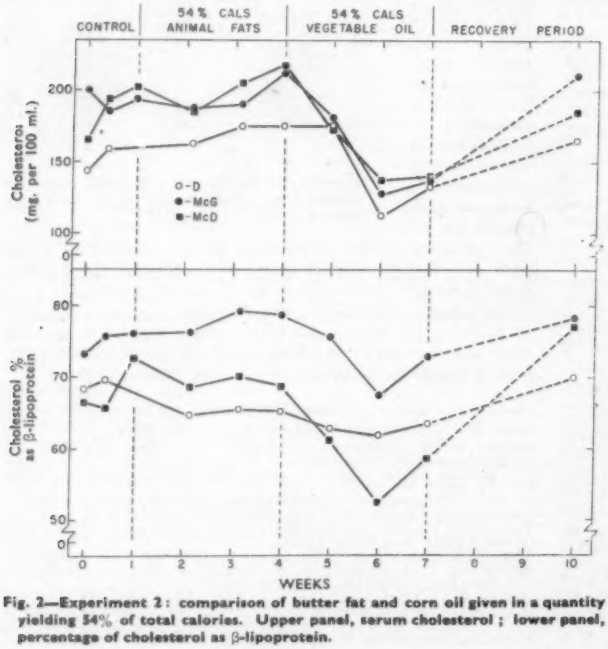

Fig. 2—Experiment 2: comparison of butter fat and corn oil given in a quantity yielding 54% of total calories. Upper panel, serum cholesterol; lower panel, percentage of cholesterol as β-lipoprotein.

Procedure

The subjects were male medical students and interns in good health, who carried on with their regular duties during the experiments. During the control periods, they were allowed to select their meals ad lib in the hospital cafeteria, and their trays were checked by the dietitian who calculated from standard tables the cholesterol, the total number of calories, and the percentage of calories taken as fat, protein, and carbohydrate. During the study periods of one to three weeks, a low-fat diet was used to which the fats and fatty acid esters were added (see table).

In experiments 1 and 2, the total fat-content of the free diet was estimated from tables as providing 40% of the total calories. Subsequent chemical determinations gave a figure of 45%. In the experiments where isocaloric substitution was carried out, fat provided 40% of the total calories. With the exception of experiment 2, where some of the corn oil was given as a milk-shake, efforts were made to incorporate the fats and oils into the diet in palatable, easily digestible forms.

All diets were isocaloric for each individual, and the protein component was held constant. Subjects were weighed twice a week and attempts were made to keep body-weight constant during the experiments. Except during the period on ethyl stearate in experiment 3, there were no

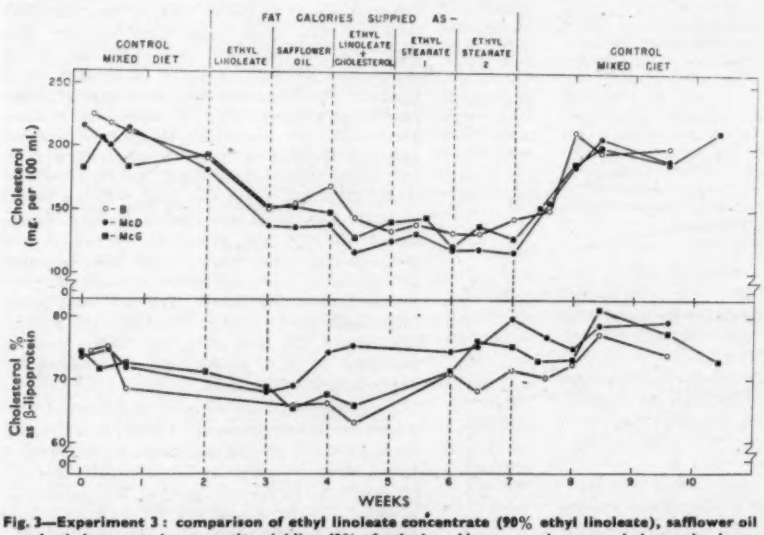

Fig. 3—Experiment 3: comparison of ethyl linoleate concentrate (90% ethyl linoleate), safflower oil and ethyl stearate in a quantity yielding 40% of calories. Upper panel, serum-cholesterol; lower panel, percentage of cholesterol as β-lipoprotein.

significant changes in body-weight. Lipids were estimated twice a week (on serum obtained when fasting); fæcal fat was estimated in experiment 5.

THE AVERAGE DISTRIBUTION OF CALORIES IN, AND CHOLESTEROL CONTENT OF, THE CONTROL AND LOW-FAT DIETS

Diet	Percentage of calories yielded			Cholesterol (mg.)
	Protein	Fat	Carbohydrate	
Control ..	14	45*	41	512
Low-fat ..	16	4*	80	28

* By analysis; all other figures from tables.

Estimations were made as follows:

Free and total cholesterol: by Sperry and Webb's (1950) modification of the Schoenheimer-Sperry method. Lipid phosphorous: by Hawk et al.'s (1947) modification of the method of Fiske and Subbarow. Lipoprotein cholesterol: in each fraction, after separation on paper by Boyd's method (1954). Fæcal fat: by the method of Van de Kamer et al. (1949).

Results

Experiment 1.—Isocaloric exchange of corn oil for the mixed fats of the free diet in 3 subjects (fig. 1). In the three-week test period, the serum-cholesterol fell 20–30% and the proportion of β-lipoprotein cholesterol by 5–10%.

Experiment 2.—Comparison of high-butter-fat and high-corn-oil diets in 3 subjects (fig. 2). Corn oil, yielding 54% of total calories, lowered the serum-cholesterol 20–30%. Butter fat raised the serum-cholesterol by 5–10%. The cholesterol/phospholipid ratio did not change appreciably with corn oil, but there was a decrease in the percentage of total cholesterol carried as β-lipoprotein.

Experiment 3.—The effect of ethyl linoleate and ethyl stearate on the serum-lipids (figs. 3 and 4). Ethyl linoleate concentrate was fed for a week, then safflower oil (at 40% of total calories) for a second week, and ethyl linoleate with 600 mg. cholesterol daily for a third week. The cholesterol level fell during these three periods, stabilising at 30–40% below the original level. At first the 3 subjects had abdominal pain and diarrhœa, but this settled down by the end of the first week. They did not lose weight. Biochemical studies showed considerable metabolic disturbance during the first week, with a rise in the ratio of free to total cholesterol and of cholesterol to phospholipid (C/P) (fig. 4). There were variable changes in the percentage of cholesterol carried as β-lipoprotein. The disturbance in C/P ratio had subsided by the end of the week on safflower oil, and did not recur during the experiment.

Ethyl stearate (40% of calories) was then substituted for the ethyl linoleate for a two-week period. The serum-cholesterol did not change from the low levels reached on linoleate, but the percentage of cholesterol as β-lipoprotein rose to the control levels in the 2 subjects in whom it had fallen. The stearate was not well absorbed, as was evident from a loss in body-weight and a change in the character and bulk of the stools. Later studies (experiment 5) showed that 65–70% of ethyl stearate was absorbed when it contributed up to 25% of the calories, and that ethyl linoleate was relatively well absorbed (fig. 6).

Experiment 4.—The effect of ethyl-linoleate concentrate on the serum-lipids following ten days on a low-fat diet in 3 subjects (fig. 5). The low-fat diet (10 g. a day of mixed fats, yielding 4% of total calories) led to falls of 30–40% in the serum-lipids in ten to fourteen days.

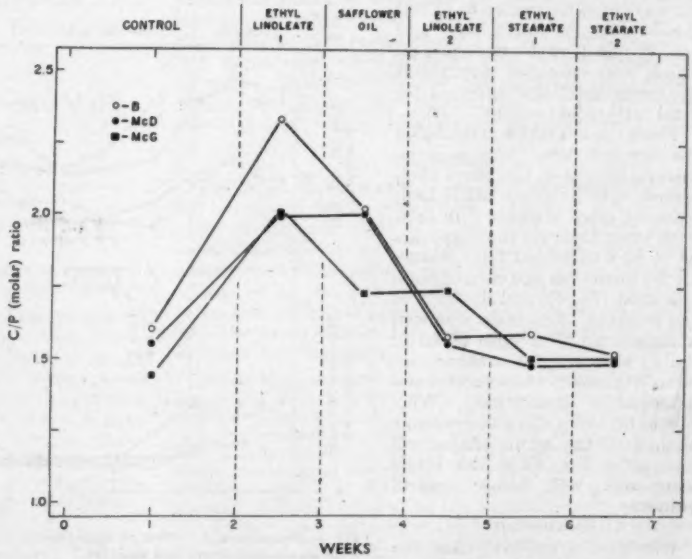

Fig. 4—Experiment 3: serum-cholesterol/phospholipid ratios.

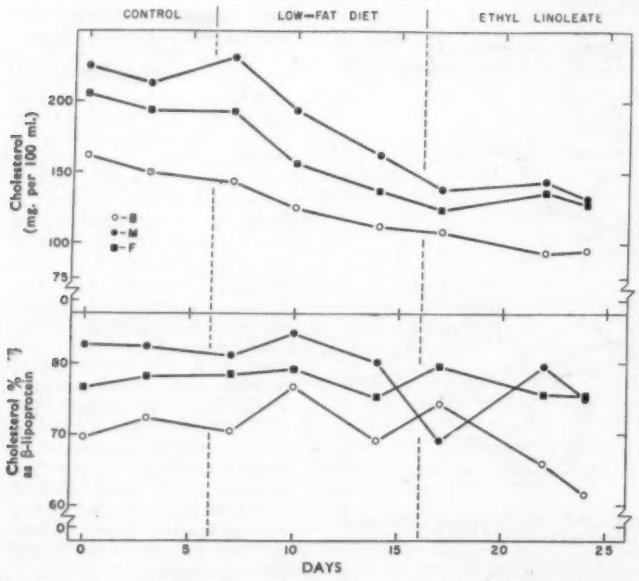

Fig. 5—Experiment 4: effect of ethyl-linoleate concentrate on the serum-cholesterol following a preliminary period on the low-fat diet.

The addition of ethyl linoleate yielding 40% of the calories did not result in any further fall in serum-cholesterol. Fluctuations in β-lipoprotein cholesterol were not consistent.

Experiment 5.—Ethyl linoleate, ethyl stearate, corn oil, and butter fat, were severally fed to each of 4 subjects at the end of two weeks on the low-fat régime (fig. 6). The fats and oils were added to the diet in increments of 10 g. every three days, except butter fat, which was given in increments of 20 g. By the end of the experimental period, the subject on butter fat was receiving 80 g. of added fat daily. while the other three subjects were receiving 70 g. The proportion of total calories yielded was 26·4% for butter fat, 23·7% for corn oil, 25·2% for linoleate, and 25·7% for stearate. The added fat was given for twelve days (for the subject on butter fat) and twenty-one days (for the other 3). Stools were collected throughout the experiment and analysed for total fatty-acid content.

From the low levels attained on the low-fat diet, there was no discernible rise in the blood cholesterol with corn oil, ethyl linoleate, or ethyl stearate: in fact, with ethyl stearate there appeared to be a sustained fall. Nearly all the butter fat and corn oil were absorbed (fig. 6), and 65–70% of the stearate. Linoleate was well absorbed up to a dose of 60 g. daily; when the dose was increased to 70 g., there was a substantial decrease in absorption. With butter fat there was no significant change in the serum-cholesterol and after ten days the levels were still well below control values.

Discussion

Our results indicate that the serum-cholesterol could be reduced about equally well by the elimination of fat from the diet or by the ingestion of either corn oil or ethyl linoleate. Ethyl linoleate was not well tolerated at first, resulting in transient diarrhœa and a rise in the C/P ratio. Ethyl linoleate did not seem to have any special depressant effect on the serum-cholesterol over and above that which could be observed by removal of fat from the diet. When ethyl stearate was given in doses up to 70 g. daily, about 65–70% was absorbed. When it was given in large amounts (40% of calories) after two weeks on a low-fat diet it did not alter the serum-cholesterol levels. When it was given after three weeks of ethyl linoleate, the serum-cholesterol did not alter, but there was an increase in the percentage of cholesterol carried as β-lipoprotein.

Our results do not support the concept proposed by Beveridge et al. (1956b) and Bronte-Stewart et al. (1956) that highly unsaturated fatty acids specifically depress the serum-cholesterol. In Beveridge et al.'s experiments (1956a), the period of low-fat feeding before feeding corn oil was too short to eliminate the possibility that the further fall in cholesterol was due to a carry-over of the low-fat effect. In Bronte-Stewart et al.'s experiments (1956), corn oil did not depress the already low serum-lipids of the Bantus, but did depress the higher levels in Europeans. This is consistent with our results. Highly unsaturated fish oils did depress the serum-cholesterol in both Europeans and Bantus.

The effect of ethyl stearate is difficult to explain. Tsung-min Lin et al. (1955, 1956) have shown, in the rat, that feeding palmitic acid or tri-elaidin, with extra cholesterol, resulted in increased fæcal cholesterol excretion. Palmitic and stearic acid also resulted in a large increase in cholesterol excretion in rats on cholesterol-free diets. Thus, in rats, palmitic and stearic acid can increase the excretion of cholesterol, whether of dietary or endogenous origin. The mechanism of action is unknown, but interference with esterification of cholesterol or its solution and removal in the unabsorbed residue of the fat could be a factor.

It is conceivable that fatty acids of different chain lengths and degrees of saturation may have conflicting effects on

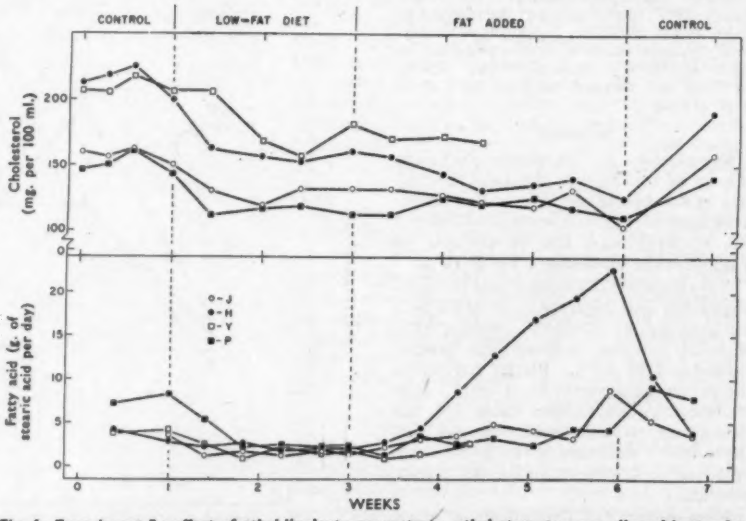

Fig. 6—Experiment 5: effect of ethyl-linoleate concentrate, ethyl stearate, corn oil, and butter fat on serum-cholesterol and stool fat. J received ethyl linoleate, H ethyl stearate, P corn oil, and Y butter fat.

cholesterol synthesis in the body. Wood and Migicovsky (1956) reported that fatty acids inhibit the incorporation of ^{14}C-labelled acetate into cholesterol in rat liver homogenates. Inhibition increased as chain-length rose to C_{12} and then abruptly fell off. Fatty acids with odd numbers of carbon atoms in the chain, and unsaturated fatty acids, appeared to possess remarkable inhibitory properties. This would suggest that, at least in the rat, when the diet contains short-chain fatty acids (e.g., butyric) there is a "relative" acceleration of cholesterol synthesis, whereas long-chain fatty acids, especially those which are unsaturated, have a special property of inhibiting cholesterol synthesis.

Summary

In feeding experiments in healthy young adults, the serum-cholesterol was depressed equally by removing animal fat from the diet or by substituting corn oil or ethyl linoleate. After a low-fat diet or a diet containing ethyl linoleate, the serum-cholesterol was not raised by giving ethyl stearate as the principal dietary fat, though fæcal studies showed that 65–70% of it was absorbed when the amount given yielded 25% of the total calories.

We wish to acknowledge the coöperation of the medical students and interns who served as subjects in these studies. We are grateful to Miss P. Pazdry and Miss A. Dundas of the dietary department of the University Hospital who analysed and prepared the diets. Invaluable technical assistance was given by Mrs. I. Noble, Mrs. J. Murray, and Mrs. I. Warren. Mr. T. M. Mallard and Mr. L. Hoffman assisted in the preparation of the esters and oils used.

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HYDRAMNIOS AS AN EARLY SIGN OF ŒSOPHAGEAL ATRESIA

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WHEN, in 1939, the first successful operations were performed in cases of œsophageal atresia with tracheo-œsophageal fistula, the diagnosis of the condition in the newborn became a matter of practical importance. Since that time advances in surgical and anæsthetic techniques have been such that pædiatric surgeons may now reasonably expect to save half of the cases (Gross 1953, Swenson 1948). The prognosis in individual babies, however, depends on several factors, of which prematurity, associated malformations, respiratory infection, and technical operative difficulties are the chief.

In prematurity, which is a feature of about 20% of the cases (Gross 1953, Clatworthy 1955), diagnosis is often delayed and the difficulties of operation are often increased. Other malformations may accompany œsophageal atresia, but in most cases these are compatible with survival (Ingalls and Prindle 1949, Gross 1953). 90–95% of œsophageal atresias are suitable for primary anastomosis, but the technical difficulty of the operation varies according to the type of deformity. Though this must make some contribution to the total mortality, it is respiratory infection, in the form of inhalation pneumonia, which accounts for most of the deaths. Figures for this are lacking in the larger reported series, but from a collective analysis of several smaller groups, reported in greater detail, respiratory infections seem to be responsible for 70% of deaths in patients who are operated on (Belsey and Donnison 1950, Otterdoom 1954, Krauss and Betke 1955).

For the present, prematurity and associated malformations are beyond our control, but respiratory infections are largely preventable if the diagnosis is made early and appropriate prophylaxis begun while operation is being arranged. It is the obstetrician who has the best chance of making an early diagnosis, and the purpose of this communication is to emphasise that in most cases he may be able to suspect it even before the baby is born.

Clinical Review

In the eight years 1948–55, 13 cases of œsophageal atresia were seen in the practice of Mill Road Maternity Hospital, Liverpool, where, on average, 3500 babies are born each year. This gives an incidence of about 1 in 2000 births; but in the earlier years several babies died who may have had the condition but did not come to necropsy, so the true figure is probably in the region of 1 in 1500 births. This would agree with the estimate of Cieters and de Rom (1955), but Belsey and Donnison (1950) found 1 case in every 800 births. Since, for one reason or another, all our cases of œsophageal atresia died, the incidence can be given more strikingly by saying that 1 in every 42 neonatal deaths in the period was due to œsophageal atresia.

During the same period in the same hospital, hydramnios was diagnosed in 169 cases. The criteria which we accepted for this diagnosis were either (1) the recording of clinical evidence of an excess of liquor by independent observers on separate occasions during late pregnancy, or (2) the recovery of more than 1500 ml. of liquor at amniotomy.

In 54 out of 169 cases (32%) the excessive accumulation of liquor may be ascribed to conditions in which there was probably a failure of the fœtal swallowing-mechanism (anencephaly 32, œsophageal atresia 12, duodenal atresia 3, iniencephaly 2, gross hydrops fœtalis 4, and eventration of diaphragm 1). Among these were 12 of the 13 babies who had œsophageal atresia and 4 babies with other obstructive anomalies of the upper digestive tract of a type amenable to surgery.

Discussion

The origin and disposal of liquor amnii have long been the subject of much contentious argument, but the one route of disposal which is known with certainty is the fœtal alimentary tract. Evidence of this is the constant finding of skin debris and lanugo in the fæces of normal infants or in the gut of stillborn fœtuses at necropsy. It has also been shown repeatedly that substances injected into the amniotic sac can later be found in the fœtal stomach and intestines.

This is illustrated by a radiograph obtained several years ago during amniography for the purpose of determining the position of the placenta. 40 ml. of 50% diodone was injected into the amniotic sac, and the subsequent radiograph shows that, besides the diffuse shadow of the opaque medium in the liquor surrounding the fœtus, there is a denser shadow of swallowed liquor in the fœtal stomach (fig. 1). That the ingested material passed along the alimentary tract while the fœtus was still in utero is shown by the shadows in the terminal gut when the fœtus was X-rayed immediately after delivery several days later (fig. 2).

Textbook lists of possible causes of hydramnios are usually comprehensive but unreasoned, and they lack the sequence necessary to guide the clinician. This has tended to obscure the simple and not surprising fact that *excessive liquor accumulates most consistently in states which render the fœtus mechanically or neurologically incapable of swallowing or absorbing it.* As mentioned, such states were the cause of hydramnios in about a third of the cases in this series.

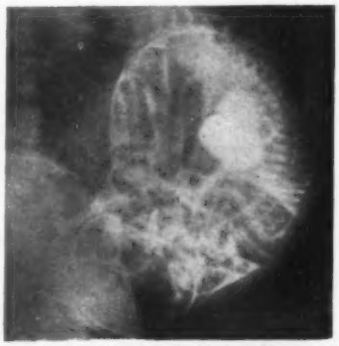

Fig. 1—Amniogram showing evidence of fœtal swallowing. The large opacity is due to the presence of ingested liquor in the baby's stomach.

Anencephaly may prevent swallowing, either because of the defect in the brain or because of the attitude of the head on the trunk. Amniography was done in 4 cases in which the fœtus had appeared anencephalic on antenatal radiography. 3 of these cases had well-marked hydramnios, and in them the radiographs showed no evidence of fœtal swallowing. In the 4th case, the amount of liquor appeared normal and the radiograph showed that this fœtus *was* swallowing the liquor (fig. 3). That it was able to do so was explained by the finding, after delivery, that it had a moderate amount of brain tissue and that the condition was one of gross encephalocele rather than of anencephaly. In the cases of severe hydrops fœtalis, the lips, tongue, cheeks and fauces were so œdematous that swallowing must have been impossible (fig. 4.) It was only when the circumoral swelling was gross that we encountered hydramnios with hydropic babies. In such cases, care is necessary to ensure that the abnormal bulk of the fœtus and its placenta does not lead to a mistaken diagnosis of hydramnios; in those to which we refer, a measured amount of more than 3 pints of liquor was released at amniotomy.

Fig. 2 (same case as fig. 1)—Radiograph of fœtus after delivery, showing the opaque material in the large bowel.

Of the 13 cases of œsophageal atresia, hydramnios was present in 12. Its absence in the remaining case only goes to emphasise the association and its mechanism, for in this particular fœtus, necropsy revealed the extremely rare type of malformation in which both segments of the œsophagus communicate with the trachea. This provides a route by which swallowed liquor may pass to the lower, absorptive levels of the alimentary tract. In view of the evident cause-and-effect relation between fœtal swallowing defects and hydramnios this common coexistence of œsophageal atresia and hydramnios is not surprising. It *is* surprising, however, to find how rarely the association is acknowledged and, when it is mentioned, how little importance is attached to it (Ingalls and Prindle 1949, Otterdoom 1954, Clatworthy 1955). That prematurity is common where the infant has œsophageal atresia was noted by Gross (1953) and Clatworthy (1955), but the deduction that the premature labour results from a coexisting hydramnios does not seem to have been made.

One reason why the relation between hydramnios and œsophageal atresia has rarely been recognised probably is that most of the published papers are by surgeons and pædiatricians, who may not always have had detailed antenatal notes at their disposal. In all our cases, the mothers had had regular antenatal care at the hospital.

Fig. 3—Postnatal radiograph of fœtus after amniography. There is evidence that radio-opaque liquor has been swallowed by the fœtus.

The appearance of swallowed liquor was unexpected in this case, for a previous radiograph had shown what was thought to be an anencephalic fœtus. After delivery of the fœtus it was seen that the abnormality was a gross encephalocele, not anencephaly; the bulbar swallowing mechanism was therefore presumably intact.

After we had come to appreciate the close association, Cieters and de Rom (1955) published their series of 10 cases of œsophageal atresia, in all of which hydramnios had been noted during the antenatal period, and suggested a scheme of management for hydramnios similar to that which we were already practising and of which details are given below. Rossier (1955) also recognised the association and its importance.

Fig. 4—Case of severe hydrops fœtalis. The gross œdema of the mouth and surrounding parts is sufficient to interfere with swallowing and result in hydramnios.

The Management of Cases of Hydramnios

When hydramnios is diagnosed, current procedure is to X-ray the mother's abdomen to exclude gross malformation of the fœtus, especially anencephaly. If no such abnormality is found, the usual policy is to keep careful watch lest mobility of the fœtus give rise to malpresentation in labour, or prolapse of the cord be brought about by the rush of waters when the membranes rupture. Some obstetricians fear that the sudden loss of liquor

will precipitate abruptio placentæ, while others fear uterine inertia and possibly third-stage troubles. These hazards past, however, the obstetrician tends to regard the case as normal, while the pædiatrician (if he is informed that hydramnios has been a feature) does not attach much significance to it once he sees that there is no *obvious* malformation in the infant. The following case is illustrative, the fatal outcome being particularly tragic because a cardiac lesion had made the mother an obstetric cripple.

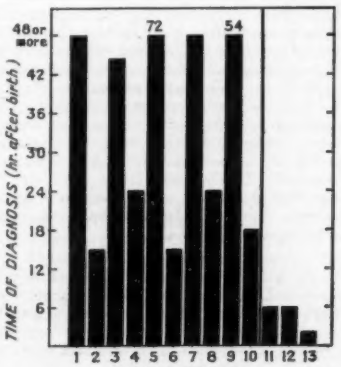

Fig. 5—Age of infants at time of diagnosis of œsophageal atresia.

The thin line between cases 10 and 11 indicates the stage at which routine œsophageal catheterisation following hydramnios was instituted as a method of diagnosis.

Mrs. A's cardiac function was assessed as grade IIb (New York Heart Association Classification). She was admitted at the thirty-second week for rest in bed, and remained an inpatient until she was delivered. Considerable hydramnios was noted from about this time but no evidence of fœtal abnormality was seen on radiography. Instability of the lie caused some anxiety in the later weeks, but when labour began the fœtal head presented and a living, apparently healthy, child (weighing 7 lb. 10 oz.) was delivered with forceps under local anæsthesia. Eighteen hours after birth the baby developed tachypnœa, cyanosis, and a frothy bloodstained oral discharge. Only then was œsophageal atresia suspected and its presence established by the failure of attempts to catheterise the œsophagus. The child died during the subsequent radiological investigation of the level of the obstruction, and necropsy confirmed the diagnosis.

This case was, in fact, the one which prompted the review of these cases, and the adoption of the present policy. Thereafter, whenever hydramnios was diagnosed, the fact was entered on the *baby's section* of the case-notes and the infant's œsophagus was catheterised within a short time of birth.

The dramatic improvement, in terms of early diagnosis, brought about by this procedure, is illustrated by fig. 5. In the 10 cases before the end of 1954, the diagnosis was delayed by a period averaging over thirty-six hours, and during this time attempts had been made to feed the baby. As a result, the babies were exposed to the grave risks of respiratory infection and "drowning" by feeds. In the 3 most recent cases, œsophageal catheterisation was attempted shortly after birth merely because of the previous record of hydramnios, and in them the diagnosis was established in less than five hours—*before the first feed was given and before any signs of the disorder (such as frothy oral discharge) were evident in the baby.* A technically successful operation was carried out in all 3, but 2 died later from the effects of multiple stenoses lower down the alimentary tract, and in the 3rd a breakdown of the anastomosis on the tenth day was the cause of death.

In skilled hands, the passage of a rubber catheter into the stomach of a newborn infant cannot be regarded as dangerous: indeed, it is entrusted to sisters in charge of the feeding of premature babies. For the purpose of diagnosing œsophageal atresia, the catheter needs to be fairly firm, as a soft catheter may coil up in the upper œsophageal pouch (which is often capacious) and thus mislead the observer into believing that it has passed to the stomach. Any doubt, however, may be easily resolved by the detection of fremitus produced in the epigastrium by a little oxygen bubbled through the catheter into the stomach. In our experience, with a no. 12 catheter this is not usually necessary, for the catheter tip can be felt on simple epigastric palpation, once it has passed into the stomach. When such a catheter fails to pass easily into the stomach of a baby born out of a hydramniotic sac, the diagnosis of atresia is sufficiently certain to warrant immediate transfer of the baby to a neonatal-surgery unit.

The benefits of this routine are:

1. It allows the diagnosis to be made immediately or very soon after birth and before the onset of secondary ill effects.
2. Attempts at oral feeding, with the attendant dangers of drowning and respiratory infections, are not made.
3. Continuous drainage of the upper œsophageal pouch can be started to avoid seepage of pharyngeal fluid into the trachea.
4. The patient can be nursed and transported in the posture most likely to reduce regurgitation from the stomach. With the commonest type of anomaly, this is the semi-erect position, which prevents stomach secretions from draining into the lungs by way of the low tracheo-œsophageal fistula.
5. Antibiotics can be administered from the beginning to guard against the otherwise inevitable pulmonary infection.

As a result, the surgeon is presented with a patient much better fitted for the major operation which is necessary. In the series of Koop et al. (1954) the mortality-rate was 78% when diagnosis was delayed beyond seventy-two hours and 42% when the diagnosis was made sooner. It is true that the group in which diagnosis is late may be weighted by a higher proportion of premature babies, in whom, because of reduced secretory activity and later feeding, the appearance of the classical signs is delayed. Nevertheless, for a considerable number of bigger babies, inhalation pneumonia will cause death.

Impressive as the earlier diagnosis of the recent cases may be, it is by no means the best which can be achieved. Credit for the earliest diagnosis must be given to de Snoo, who, in 1937, made an *antenatal* diagnosis of œsophageal atresia after noticing that saccharine, which he injected into the amniotic sac, appeared in the maternal urine in all cases except one; he concluded that the fœtus in this case could not swallow and an infant with œsophageal atresia was eventually delivered. de Snoo's method is unsuitable for routine use because of the technical difficulties of the analysis. A simpler test based on the same principle could probably be devised; but, it is doubtful whether antenatal diagnosis has any real advantage over diagnosis immediately after birth.

If the passage of a catheter is obstructed, confirmation of the obstruction and localisation of its level can be obtained *after* transfer to the surgical unit. Belsey and Donnison (1950) point out that this saves time and avoids repetition of X-ray examinations.

Of the 169 cases of hydramnios, 119 were not explained by immediately obvious abnormalities or œsophageal atresia. In this whole series, therefore, 1 case of œsophageal atresia would have been revealed in every 10 routine catheterisations of infants born from hydramniotic sacs. These figures are in keeping with the estimate of Carvalho (1954), who calculated that, in 1 out of 12 cases, hydramnios is due to œsophageal atresia. In the remaining cases it would still have been unwise to conclude that the alimentary tract was normal, for some of them had duodenal atresia or diaphragmatic hernia, both of which are amenable to surgery. Continued close observation is therefore essential to ensure that such conditions shall not be overlooked (Castanier et al. 1955). It must also be borne in mind that cases of the type in which both œsophageal pouches communicate with the trachea are unlikely to present with hydramnios, and the diagnosis in these circumstances will probably be impossible until secondary signs of the lesion appear in the neonatal period.

Summary and Conclusions

The alimentary tract of the fœtus is the most important route of disposal of liquor amnii and defects in the

swallowing mechanism are prominent among the causes of hydramnios, accounting for about a third of the cases reported here.

If antenatal observation is strict, hydramnios is found as an almost constant accompaniment of œsophageal atresia, as in 12 of the 13 cases in the present series. The malformation will usually be diagnosed at birth if an attempt is made to pass a rubber catheter into the stomach of an infant born from a hydramniotic sac. In the series reported, the adoption of this procedure shortened the average interval between delivery and diagnosis from thirty-six hours to less than five hours. Early diagnosis reduces lung complications and brings the patient to operation in good condition.

The adoption of this simple measure by all obstetricians could lead to further considerable improvement in the results of surgery for high congenital lesions of the alimentary tract in the newborn child.

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CARDIAC INVOLVEMENT IN ANAPHYLACTOID PURPURA

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THE histological lesion in anaphylactoid purpura is a peri-angiitis of arterioles and capillaries (Gairdner 1948). The inflammation is transient but liable to recur, and it leads to the formation of papules, petechiæ, and urticarial œdema. These characteristic changes are found in symmetrical areas of the skin, in the intestine, and around joints. Minor trauma may be responsible for the appearance of visible lesions at these sites, but the process is more widespread than this because the kidney glomeruli are also often involved. Lesions in other viscera are rarely found, perhaps because the primary condition is no longer active in patients dying of complications. Involvement of the nervous system (Lewis and Philpott 1956) and, in one instance, focal necroses of the myocardium (Lecutier 1952) have, however, been described.

We report here three cases in which there was clinical and electrocardiographic evidence of myocardial damage during attacks of anaphylactoid purpura.

Case-reports

THE FIRST CASE

A housewife, aged 72, developed colicky abdominal pain in January, 1955. Appendicitis was suspected, but at laparotomy subserosal hæmorrhages were found along the terminal ileum. The patient complained of substernal discomfort for a few days after the operation. She had further colic at infrequent intervals during the next year, and in August, 1956, she returned to hospital in a prolonged attack. She had suffered intermittent pain for three weeks and, when it was present, could feel a lump in the right side of her abdomen. During the first week she also had hæmaturia, vomiting, and slight hæmatemesis. In the past three days she had severe retrosternal discomfort, which was continuous and did not radiate elsewhere. Cardiac infarction was suspected, and the patient was admitted to hospital.

Condition on Admission

She was apyrexial but looked ill and was slightly dyspnœic. Her blood-pressure was 150/60 mm. Hg and her venous pressure was high. Her pulse was irregular, but there were no signs of cardiac enlargement, and no murmurs or extra sounds were heard. Her heart-rate was 110 but at times it fell to 40 and became regular. Stokes-Adams attacks occurred at short intervals. In addition she had a symmetrical rash which was purpuric on her buttocks and thighs and papular on her elbows. She had noticed the rash intermittently for two years, and on this occasion it had just appeared. The crops of spots did not always coincide with the attacks of colic. When the spots were present, her hands were sometimes swollen. A tourniquet test was negative, but fresh papules appeared on the following day distal to where the cuff was applied. Her urine contained albumin and a few red blood-cells but no casts. No other abnormalities were found.

Investigations

Hæmoglobin 72%; white blood-cells 9000 per c.mm.; platelets 300,000 per c.mm., L.E. cells absent; erythrocyte-sedimentation rate (E.S.R.) (Westergren) 82 mm. in one hour; blood-urea 103 mg. per 100 ml.; serum-albumin 3·3 g. per 100 ml.; serum-globulin 4·5 g. per 100 ml.; antistreptolysin and differential agglutination titres normal; fæcal occult blood absent. Radiography of the chest showed clear lung fields and slight enlargement of the heart.

Progress

The Stokes-Adams attacks ceased after the patient was given morphine and ephedrine. Her venous pressure fell to normal two days later, and her pulse became regular on the ninth day. Two further episodes of arrythmia occurred in the third week, the first of which was accompanied by syncope and vomiting. The purpura waxed and waned for a week and then faded completely. There was no further colic or vomiting. The blood-urea level rose to 131 mg. per 100 ml. in the second week but had fallen to 41 mg. per 100 ml. when the patient was discharged four weeks later. Her urine then contained no albumin or red cells, and her blood-pressure was 170/90 mm. Hg. A month later she was symptomless, although the rash had recurred. Her pulse was regular and blood-pressure unchanged. Exercise tolerance was normal, and there were no signs of cardiac failure. Her hæmoglobin was 79%, E.S.R. 26 mm. in one hour, and blood-urea level 48 mg. per 100 ml.

Electrocardiography

Serial records showed three abnormalities (fig. 1). The pattern of the QRS complexes, which remained constant throughout the period of observation, suggested the presence either of a healed anteroseptal infarct or of biventricular

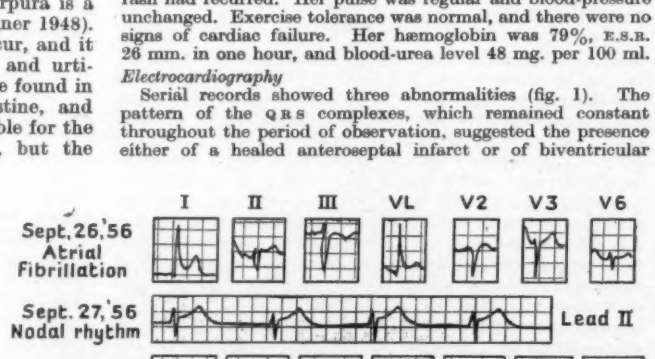

Fig. 1—Electrocardiograms of case 1, showing alterations of rhythm and sequential changes in ST-T segments. First record was obtained on admission to hospital.

hypertrophy. Atrial fibrillation was present on admission and recurred twice before being permanently superseded by sinus rhythm. Nodal rhythm also was recorded when the syncopal attacks were occurring. Finally, there were widespread changes in the ST-T segments, which reverted to normal after five weeks. At first, upright T waves with ST raised in leads I, VL, and V_6 were shown. Later the ST segments became isoelectric and the T waves shallowly inverted in leads I, V_{1-7}, and VL. At no time were the Q waves of classical infarction found.

The only clinical detail with which the permanent Q R S change could be correlated was the substernal pain which occurred after laparotomy in the first attack of colic. Electrocardiograms were not obtained during this incident, but it may well have been cardiac infarction since the blood-pressure was later found to be lowered. The temporary arrhythmias and sequential changes in the ST-T complexes suggested diffuse myocardial injury.

This case showed the typical features of anaphylactoid purpura involving the skin, small gut, and kidneys. Laparotomy was performed in the first attack, which was apparently complicated by cardiac infarction. During a recurrence nearly two years later, evidence of temporary myocardial damage coincided with renal and intestinal involvement. Despite the advanced age of the patient and the long duration of the illness, both the cardiac and the renal failure resolved spontaneously. The attacks of purpura were not related to the ingestion of any particular food, although persistence of the syndrome for several years is said to increase the likelihood of this.

Myocardial damage was clinically obvious in this patient, but the electrocardiographic changes were somewhat indeterminate. In case 2 the electrocardiographic abnormality was more striking.

THE SECOND CASE

An Irishman, aged 53, had a posterior cardiac infarct in December, 1952. After this he remained well until November, 1956, when he began to have muscle pains and a productive cough, with slight hæmoptysis. Three days later he suddenly became breathless, and next day he noticed a rash on his limbs. He was found to have atrial fibrillation (pulse-rate 110) and was referred to hospital.

Condition on Admission

He had no angina or abdominal pain, but had lost 7 lb. in weight. His temperature was 99·5°F, and he had symmetrical purpura on his shoulders, arms, buttocks, and legs. His pulse was regular, pulse-rate 94, and jugular venous pressure not increased. A third heart sound was present, but there were no murmurs or signs of cardiac enlargement. The blood-pressure was 90/50 mm. Hg, the urine was free from albumin and red cells, and no other abnormalities were found.

Investigations

Hæmoglobin 96%; white blood-cells 6000 per c.mm.; platelets 155,000 increasing to 306,000 per c.mm.; L.E. cells absent; E.S.R. (Westergren) 20 mm. in one hour; serum-albumin 4·4 g. per 100 ml.; serum-globulin 4·4 g. per 100 ml.; blood-urea 27 mg. per 100 ml.; plasma-potassium 5·3 m.eq. per litre. Straight radiography and tomography of the chest showed an extensive fibrotic lesion of the right upper lobe. No cardiac enlargement. Sputum culture repeatedly positive for tubercle bacilli. Mantoux test positive (1 : 1000 dilution).

Progress

The pyrexia and rash disappeared in eight days. The tourniquet test was positive for eight weeks, however, and for a fortnight application of the cuff caused reactivation of the Mantoux response. The patient gained weight and was no longer breathless, and the lung lesion regressed, after treatment with anti-tuberculous drugs. Eight weeks after admission the third heart sound was inaudible, the blood-pressure was 125/70 mm. Hg, the E.S.R. was 4 mm. in one hour, and the blood-urea level was 31 mg. per 100 ml. The urine remained free from albumin, and there was no colic.

Electrocardiography

The record (fig. 2) in 1952 was typical of posterior infarction. That obtained two days after the onset of purpura showed ST raised in leads II, III, and VF, and deep inversion of the T waves in all the chest leads. Inversion of T_3 and T_{VF} followed two days later. These changes gradually disappeared in the next eight weeks. Sinus rhythm was shown in all the

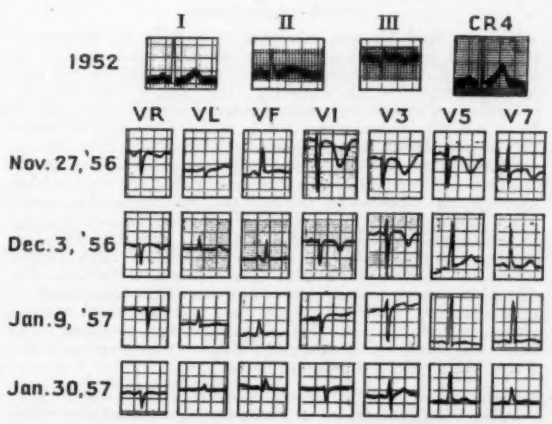

Fig. 2—Electrocardiograms in case 2: tracing in 1952 shows posterior cardiac infarct; later records show gradual resolution of widespread T-wave changes. Purpura appeared on Nov. 25, 1956.

records, but none was obtained initially when the pulse was irregular. The abnormality in this case suggested diffuse temporary subepicardial damage.

The association of anaphylactoid purpura with pulmonary tuberculosis is recognised (Dalgleish and Ansell 1950), and it has been suggested that tuberculin may be an allergen in such cases (Ellman and Johnson 1952). The characteristic rash appeared in this patient when there was clinical and radiological evidence of reactivation of the lung infection. Also the duration of the purpura was brief, which is usual in tuberculosis. A positive tourniquet test and a slight decrease in the platelet-count are occasional findings in this variety of purpura. The electrocardiographic abnormality was more definite than that found in case 1, and it again suggested diffuse myocardial damage. As in case 1, it was maximal at the onset of the purpura and disappeared several weeks later. This patient showed definite evidence of previous cardiac infarction, but the later electrocardiographic changes were unlike those of a further cardiac infarct. Tuberculous pericarditis was excluded on clinical grounds. Most significantly there was no obvious renal involvement in this case; therefore the electrocardiographic changes could not be ascribed to the "nephritis" of anaphylactoid purpura. Very similar changes are nevertheless known to take place sometimes in the course of acute glomerulonephritis (Wood 1956).

Electrocardiographic changes were also found in case 3, who died of progressive renal failure. Clinical evidence of myocardial damage was minimal in this case.

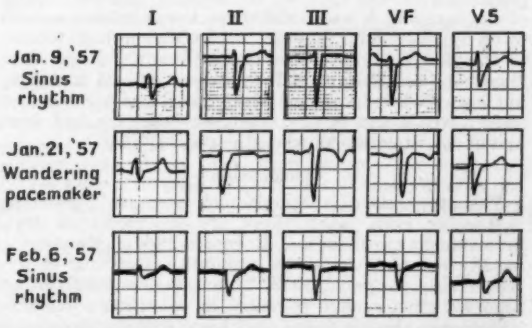

Fig. 3—Electrocardiograms of case 3, showing alteration of rhythm and inversion of T_3 and T_{VF}, which coincided with recurrence of purpura.

THE THIRD CASE

A man, aged 77, was admitted to hospital in December, 1956, with infected varicose eczema. He had generalised dermatitis but was otherwise well. His pulse-rate was 80, and blood-pressure 170/100 mm. Hg. He had a basal systolic murmur but no obvious valve lesion or cardiac enlargement. The E.S.R. (Westergren) was 5 mm. in one hour, and his urine did not contain albumin or glucose. The rash rapidly improved with local treatment, but after two weeks the patient developed anorexia and a burning substernal pain. Three days later albuminuria appeared for the first time and occult blood was found in the fæces. The dermatitis remained healed, but two days later profuse purpura appeared on his arms, buttocks, and thighs. The rash was not present on his face or trunk, except where an adhesive plaster had been applied. It faded in five days, but a fresh crop appeared a week later accompanied by mild epistaxis. The tourniquet test was positive for three weeks, and albuminuria (Esbach test 4–10 *g.*) persisted. The urine was sterile on culture and contained many red cells and a few white cells and granular casts.

Investigations

After the development of the purpura examination of his blood showed hæmoglobin 79%; white cells 12,000 per c.mm.; platelets 264,000 per c.mm.; L.E. cells absent; E.S.R. 18 mm. in one hour; blood-urea 139 mg. per 100 ml.; serum-albumin 2 g. per 100 ml.; serum-globulin 3·3 g. per 100 ml. Radiography of his chest showed clear lung fields and slight cardiac enlargement.

Progress

The patient became increasingly œdematous, and a transient increase in his jugular venous pressure was noted at the onset of the second attack of purpura. The heart sounds and blood-pressure were unchanged, and the purpura disappeared in five days. Gross albuminuria continued, and the patient died, severely acidotic, three weeks later. A week before death his E.S.R. was 30 mm. in one hour; blood-urea 120 mg. per 100 ml.; serum-albumin 1·8 g. per 100 ml.; and plasma-potassium 5·7 m.eq. per litre.

Electrocardiography

The first record (fig. 3) was obtained on the day that albuminuria appeared. It showed an r^s pattern in leads V_{5-7} which persisted until the patient's death. At the onset of the second attack of purpura a wandering pacemaker and sharp inversion of T_{V5} and T_3 were shown. The T waves became upright, and sinus rhythm was re-established, four days later. Subsequent records remained unchanged.

The significance of the abnormal Q R S pattern remains uncertain, because there were no earlier electrocardiograms. The transient T-wave changes suggested localised myocardial damage.

Post-mortem Findings

The heart weighed 480 g. but was otherwise normal. Both kidneys were pale and enlarged, and their capsules stripped easily. The other viscera appeared healthy, and no petechiæ were seen, although there was generalised œdema. Histologically the kidneys showed the appearances of glomerulonephritis in an early subacute phase, and no lesions were found in the heart.

This case followed the typical course of anaphylactoid purpura when the kidneys are severely affected. None of the drugs with which the eczema was treated seemed to be responsible for its onset, which was perhaps related to the skin infection. The cardiac manifestations were transient, and they would have been missed had they not been looked for specifically. No histological abnormality was found in the heart, but purpura had been absent for three weeks when the patient died.

Discussion

The prognosis of anaphylactoid purpura is generally favourable even when there are symptoms of renal involvement (Derham and Rogerson 1956). Recovery is usually complete in about a month, after four or five recurrences (Ackroyd 1953). Nevertheless fatalities are reported often enough to make the condition potentially dangerous. Complications arise because the inflammation is unduly severe or because it continues to recur for an unusually long time. In either event death commonly results from progressive renal failure. It is uncertain whether the renal lesion in fatal cases is an associated glomerulonephritis or simply the end-result of the original angiitis. Other organs besides the kidney may be seriously affected, and the lesion is then sometimes found to be due to exceptionally severe angiitis. Necrotising arteriolitis, for example, has been observed in association with ulceration of the skin and intestines, and very rarely periarteritis nodosa is discovered (Gairdner 1948). Convulsions, hemiplegia, and subarachnoid hæmorrhage are other unusual complications of this disorder. Lecutier's (1952) case, however, appears to be the only one in which involvement of the heart is reported, and in his patient the lesions were discovered post mortem.

In the present cases the cardiac manifestations were remarkably alike. In two of them sudden symptoms and signs of cardiac failure coincided with the onset of purpura. These patients had temporary atrial fibrillation at first, and one of them also developed nodal rhythm with paroxysmal heart-block. The third case developed a transient increase in venous pressure and a wandering pacemaker during a recurrence of purpura. Electrocardiography showed sequential changes in the ST-T complexes, which were widespread in two cases and localised in the third. The complexes returned to normal within a few weeks in two cases, and within a few days in the third. In two cases the attack began with retrosternal pain, but in the other it was painless. The patients were elderly, and two had clinical evidence of a healed cardiac infarct. Serial electrocardiograms did not, however, support the suggestion that their illness had simply provoked a coronary thrombosis. Moreover in one patient it seemed likely that the original infarct occurred during an earlier attack of purpura. The electrocardiographic changes resembled those which are sometimes found in acute nephritis, but they occurred in one case in the absence of renal involvement. There was no clinical evidence of periarteritis nodosa or of rheumatic heart-disease, which very rarely may be associated with anaphylactoid purpura (Gairdner 1948). It thus appears likely that the observed changes were due to direct involvement of the heart by the inflammation rather than to secondary effects of its presence elsewhere.

Anaphylactoid purpura is usually considered to be an allergic vascular reaction, although the responsible agent is only identified in a minority of cases (Ackroyd 1953). It is therefore significant that the cardiac changes in these three cases were not only similar to those of nephritis but also closely resembled those known to occur in serum sickness and drug reactions (Lilienfeld et al. 1950, Contro and Mond 1956). Temporary disturbances of rhythm, alterations in the ST-T segment imitating cardiac infarction, and even actual infarcts have been reported in these conditions (Roussak 1954). The fact that other allergic reactions can affect the myocardium in this manner strengthens the suggestion that the changes observed in the present patients resulted from angiitis of the heart. The same pathological process may indeed be responsible for similar changes which sometimes appear after bacterial infections in the absence of purpura. In this "post-infectious myocarditis," arrhythmias, angina, hypotension, and cardiac failure are associated with electrocardiographic evidence of temporary myocardial damage (Gore and Saphir 1947). It is also possible that the cardiac failure, which is the principal feature of "acute nephritis without albuminuria," results from the same process, although histological evidence of myocardial damage is said to be absent (Sharpey-Schafer 1955). Purpura is not invariably present in the Henoch-Schönlein syndrome, and albuminuria is often absent. Although the pathogenesis of none of these disorders is exactly known, their similarity is notable.

The heart may be affected as often as the kidneys in anaphylactoid purpura, since the vascular lesion is wide-

spread and the affected vessels are susceptible to mechanical trauma. Cardiac involvement is not likely to be so obvious as renal involvement, however, since urinary abnormalities are easily detected. The only clinical manifestation which might be expected in the average case, in which the inflammation is mild and transient, is a temporary alteration in the electrocardiogram. Electrocardiography is rarely resorted to except in the more serious cases, and in them abnormalities are apt to be ascribed to the "nephritis" which is usually present. Although the disorder is not particularly uncommon in adults, most of the published accounts are concerned with children, in whom electrocardiography is not often done routinely. Cardiac involvement may therefore be easily overlooked because, like renal involvement, it is evidently rarely serious. Nevertheless it may assume importance when the angiitis is severe or prolonged, or when the heart is already affected by degenerative arterial disease. For this reason we consider that electrocardiograms should be obtained at an early stage in every severe case and in all elderly patients with anaphylactoid purpura. Discovery of a cardiac lesion provides an additional indication for steroid therapy, since this can perhaps prevent the development of more serious changes. Such treatment is rational because it is known to lessen allergic reactions, and a preliminary report suggests that it is effective in this condition (Leese 1955). Prednisolone is probably preferably to cortisone (Cohen 1957), particularly in the presence of cardiac involvement.

Summary

Signs of myocardial damage appeared in three elderly patients with anaphylactoid purpura. The changes were transient and coincided with episodes of purpura. Temporary abnormalities in the electrocardiogram appeared in each case.

It is suggested that the cardiac manifestations were due to direct involvement of the heart by the purpuric process, and that this may happen often.

Electrocardiography may therefore be helpful in assessing the severity of the syndrome and in deciding whether steroid therapy should be used.

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Preliminary Communications

THE VALUE OF PITUITARY GONADOTROPHIN ASSAYS IN PATIENTS WITH MAMMARY CARCINOMA

GONADOTROPHIN assays may be useful in patients with mammary carcinoma for two main reasons: (1) the estimation of these hormones in urine is the only satisfactory direct measure of pituitary function at present available; and (2) on the basis of recent evidence (Loraine 1957), it seems that gonadotrophin assays may be helpful in predicting the response of some postmenopausal women with mammary carcinoma to treatment with stilbœstrol. The present communication is concerned only with the second of these clinical applications.

METHOD OF ESTIMATION OF URINARY GONADOTROPHINS

The method used in this study was described by Loraine and Brown (1956a and b). The end-point of the bio-assay depends on the enlargement of the uterus in intact immature mice. Results are expressed in terms of human menopausal gonadotrophin (H.M.G.) as H.M.G. units per 24 hours. The standard preparation used was made by Messrs. Organon (Newhouse, Scotland) and is termed 'HMG-20A.

TABLE I—URINARY EXCRETION OF GONADOTROPHINS BY CONTROLS AND BY PATIENTS WITH MAMMARY CARCINOMA BEFORE STILBŒSTROL THERAPY

Group	Response to stilbœstrol	No. of patients	Mean gonadotrophin excretion (H.M.G. units per 24 hr.)*	SD log.	Range (H.M.G. units per 24 hr.) (P = 0·95)
Mammary carcinoma	"Worse"	20	61·2	0·14	33–115
Mammary carcinoma	"No apparent change"	19	40·2	0·22	14–112
Mammary carcinoma	"Improved"	8	40·0	0·24	14–118
Controls	..	37	39·9	0·25	13–123

* The figures in this column are geometric rather than arithmetic means.

TEST PROCEDURE

Assays of pituitary gonadotrophins in urine were performed in 47 postmenopausal patients with recurrent or metastatic breast cancer before treatment with stilbœstrol. The daily output of urine was collected on each of 4–8 consecutive days. When possible, four estimations on 48-hour aliquots were made in each case, and the mean excretion value per 24 hours was calculated.

After this period of observation the patients were treated with stilbœstrol dipropionate (5 mg. twice daily by mouth) for six weeks. At the end of this time they were reviewed and were classified into three groups according to their response to treatment. These groups were designated "worse," "no apparent change," and "improved." The criteria used in this clinical classification have been described elsewhere (Strong 1957).

TABLE II—ANALYSIS OF SIGNIFICANCE OF RESULTS SHOWN IN TABLE I

Comparison	t	P
"Worse" v. "no apparent change" ..	3·04	0·01–0·001
"Worse" v. "improved"	2·66	0·02–0·01
"Worse" v. "no apparent change" + "improved"	3·80	< 0·001
"Worse" v. "control series"	3·04	0·01–0·001
"Control series" v. "no apparent change" + "improved"	0·16	0·9 –0·8

The gonadotrophin output in these patients has been compared with that in a group of 37 controls of similar age with some disease other than cancer. The complete 24-hour output of urine of each control was collected on each of four consecutive days; two estimations on 48-hour aliquots were made and the mean excretion value determined.

RESULTS

These are presented in tables I and II. It will be noted that the mean gonadotrophin excretion in the group designated "worse" is significantly higher than that in any of the other groups, including the control. Table II

shows, however, that there is no significant difference in gonadotrophin excretion between the controls and the groups classified as "no apparent change" and "improved."

DISCUSSION

These results are of interest because they indicate for the first time that the excretion of a hormone by a particular group of patients with mammary cancer may differ significantly not only from that in other groups of patients with this disease but also from that in a group of patients with diseases other than cancer. Furthermore the evidence presented suggests that gonadotrophin assays may be helpful in predicting the response of a postmenopausal patient with mammary carcinoma to treatment with stilbœstrol.

The present evidence is contrary to the observations of Segaloff et al. (1954), who claimed that a low gonadotrophin excretion by postmenopausal patients with breast cancer is usually associated with a poor prognosis. However, the assay methods used by these workers are open to criticism on various grounds, and the results they obtained probably have little quantitative significance. In our opinion it is most important that, in a study of this type, an assay method should be used which satisfies the reliability criteria described by Borth (1952); unless this is done, the results obtained are likely to mislead.

The excretion of gonadotrophins is known to decrease with advancing years. In view of this it was necessary to ascertain whether or not the factor of age alone might account for the significant differences in gonadotrophin excretion shown in table II. An analysis of co-variance was therefore undertaken in which allowance was made for the difference in age composition. The results of this analysis have been reported elsewhere (Loraine 1957); they showed that the observed differences were not due to differences in the ages of the patients.

SUMMARY

Reasonably satisfactory methods are now available for the quantitative determination of pituitary gonadotrophins in human urine. When gonadotrophin assays are used for prognostic purposes in patients with breast cancer it is essential to use methods of proved reliability.

The results presented suggest that gonadotrophin assays in urine may be helpful in predicting the response of some postmenopausal patients with mammary carcinoma to treatment with stilbœstrol.

This work forms part of a joint investigation into the endocrinology of breast cancer generously supported by the Melville Trust. In the performance of the assays the skilled technical assistance of Miss M. A. Mackay, Miss M. K. Burnett, and Miss M. R. Gillon was greatly appreciated.

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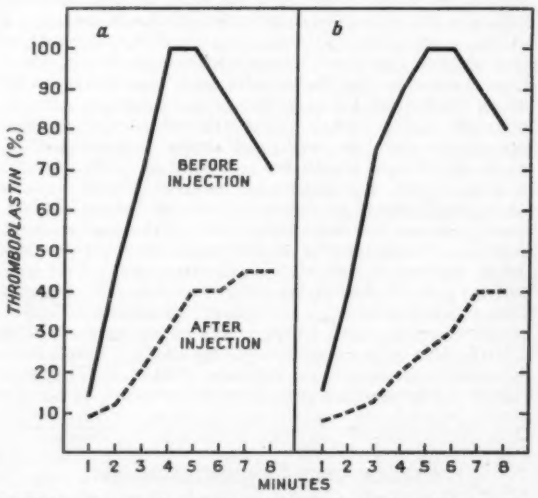
THE EFFECT OF HYALURONIDASE ON THE FORMATION OF BLOOD-THROMBOPLASTIN

To explain the results of our experiments on thrombopathy,[1–3] we tested the effect of hyaluronidase ('Kinaden,' Schering, of which one ampoule contains 10 Schering units) on the membranes of the thrombocytes and found that hyaluronidase inhibited the formation of the blood-thromboplastin both in vitro and in vivo,[4] the criterion



Inhibition of generation of thromboplastin by hyaluronidase: *a*, in vivo; *b*, in vitro.

being the thromboplastin-generation test of Biggs and Douglas.[5]

In the experiments in vitro 0·1 ml. of kinaden solution was prepared by dissolving an ampoule of kinaden in 5 ml. of physiological saline solution and added to 0·3 ml. of a suspension of thrombocytes 0·3 ml. of plasma treated with barium sulphate, and 0·3 ml. of serum.

In the experiment in vivo the thromboplastin-generation test was applied before and 20 minutes after injecting one ampoule of kinaden intravenously into a healthy person.

The results are shown in the accompanying figure.

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1. Ulutin, O. N., Karaca, M. *Bull. Soc. turq. Méd.* 1956, **22**, 473.
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5. Biggs, R., Douglas, A. S. *J. clin. Path.* 1953, **6**, 23.

"... Our approach to the problems of senescence must necessarily be in some measure subjective, as indeed are the conceptions we tend to adopt about our own place in society when we arrive at a chronologically advanced age. How subjective our approach is, we can scarcely realise, so ingrained have become our traditional habits of thought. Most of us have our words and gestures perfect as we live through the Shakespearean Seven Ages of Man. Yet a biological residue remains which is clearly entitled to be called organic ageing. What precisely accumulates or breaks down or fails to function or runs out or goes to seed, we do not know, and it may be that none of these metaphors is strictly applicable. We do not know whether we shall later find ourselves describing these experiences in neurological or biochemical or cytological terms; the chances are that no one of the biological sciences will alone prove adequate to our purpose."—F. LE GROS CLARK and N. W. PIRIE, *The Biology of Ageing*. London, 1957; p. xiv.

New Inventions

A LEG SUPPORT FOR USE DURING VAGINAL OPERATIONS

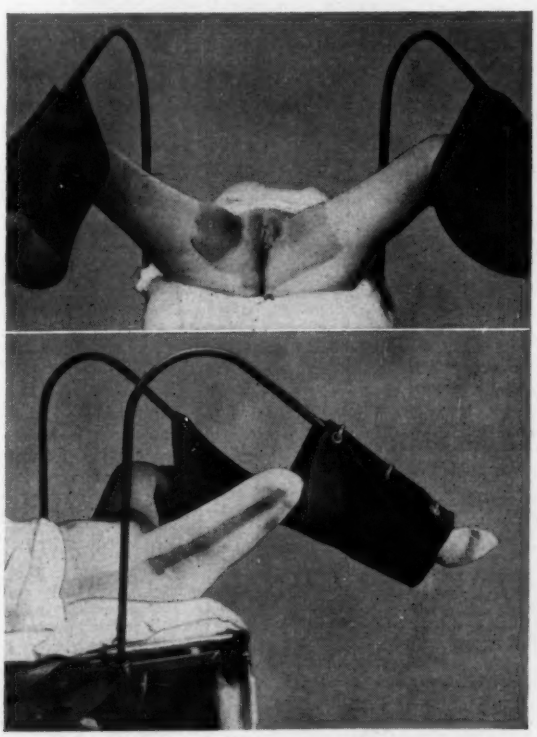
THE conventional leg-suspension apparatus for vaginal operations still leaves much to be desired. The usual arrangement of fixed upright poles, adjustable in the vertical plane only, resembles the bed of Procrustes: the patient, whether slim and long-legged or short and fat, is forced to adapt to these rigid fixtures. The result is a position of severe strain on the spine, sacro-iliac region, and the hip- and knee-joints; furthermore, respiration is embarrassed, and the venous return from the legs and pelvis is obstructed.

A new type of support has been designed which allows a relaxed position for the patient and provides ready access for the surgeon and his assistant. These points are illustrated in the accompanying figure. Sterile drapes are so arranged that the assistant works with his left arm passed between the arched support of the strut and the patient's thigh; his right arm is placed over the dependent end of the support, which also allows a clear field of vision. The sliding clamp at the side of the table regulates the degree of flexion at the hip- and knee-joints; adjustment is also possible in the vertical direction, and abduction is varied readily by swinging the patient's feet either outwards or inwards. The whole arrangement has the merit of simplicity in use.

Messrs. Chas. F. Thackray of Leeds produced the apparatus for me.

Ashton-under-Lyne General Hospital, Lancs

T. B. FITZGERALD
F.R.C.S., M.R.C.O.G.



AN ELECTRONIC NERVE-STIMULATOR

IT is now nearly nine years since Bodenham published his "calibrated electrical aid to facial nerve dissection." [1] Several instruments based on his design have been used with great success. Essentially the machine supplies high-voltage pulses at regular intervals (5–10 per second). When the pulses are fed to a surgical instrument they stimulate any motor nerve in its immediate vicinity.

The outstanding value of the stimulator is in dissections around the facial nerve, but it is also helpful in the identification of any motor nerve displaced by disease or deformity or surrounded by scar tissue. The strength of the current should be such that warning is given when the knife or scissors are about 1 mm. from the nerve; if the current is too strong, misleading contractions will occur before there is any danger of causing damage. The strength required varies very little from one patient to another; hence when the surgeon knows his instrument it can be set with confidence before operation. When several nerves have to be found, as in removal of a parotid tumour, fractional adjustment can be made if necessary after identifying the first branch. The sterile lead from the instrument is fitted with a strong clip suitable for attachment to knife, scissors, or any other instrument, so that it can be used throughout an operation, being transferred from one to another as needed.

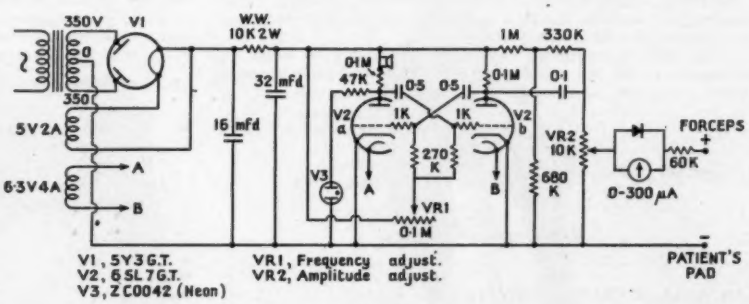


Fig. 1.

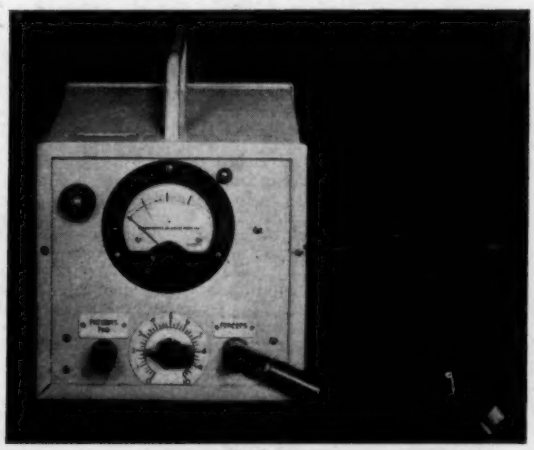


Fig. 2.

The electric-bell mechanism used by Bodenham as the core of his instrument is not ideal for the production of high-voltage pulses. Its main disadvantages are that the bell contacts become dirty and need cleaning; the apparatus must be kept level when in use; the pulse-frequency, duration, and amplitude are all interdependent, making it impossible to adjust them separately; and after prolonged use the instrument becomes erratic in operation and is difficult to restore to its original condition.

1. Bodenham, D. C. *Lancet*, 1948, ii, 975.

To overcome these difficulties an electronic model has been designed in which there is no mechanical switching. The circuit diagram is shown in fig. 1. The instrument (fig. 2) consists essentially of a multivibrator,[2] with V2a and V2b as the oscillating valves. The rapid change of anode voltage of V2b at cut-off is used to generate a voltage-pulse which is taken to the sterile lead. A neon bulb connected to the anode of V2a gives visual indication that the unit is functioning, and audible indication is given by the miniature loud-speaker in the same circuit. A small D.C. voltage is also applied to the output, to ensure that all meter readings are positive.

Frequency and amplitude are independently adjustable by potentiometers, and pulse-length could easily be made adjustable also if required. As the oscillations are purely electronic, there are no contact points to corrode. The instrument can be made small and portable but requires A.C. mains for its operation.

The first instrument of this type has now been in clinical use for ten months and, after initial adjustments were complete, has required no further attention.

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Reviews of Books

An Atlas of Cardiac Surgery

J. A. RODRIGUEZ, M.D., assistant professor of surgical anatomy and research associate, department of surgery, University of Mississippi Medical School. Philadelphia and London: W. B. Saunders. 1957. Pp. 250. £6 6*s*.

A professional anatomist and a very fine draughtsman, Dr. Rodriguez has prepared an excellent atlas. The first section, on the surgical anatomy of the heart and great vessels, sets out the important surgical topography. In preparing the more important sections on the surgery of the great vessels, cardiac valves, congenital defects, and pericardiectomy, the author spent days or weeks leaning over the shoulders of leading American surgeons; and he has recorded with accuracy and brilliant clarity, in black-and-white line drawings, their individual techniques. The concise text reflects the operator's current views and supplements each set of illustrations.

This is a very necessary book both for those directly engaged in cardiac surgery and for those keenly but less actively interested in it. No volume could represent more adequately the vision, ingenuity, and courage of the comparatively small group of workers who have made such operations possible.

Perceptual Processes and Mental Illness

H. J. EYSENCK, PH.D., professor of psychology, University of London; G. W. GRANGER, PH.D., lecturer, Institute of Psychiatry, London; J. C. BRENGELMANN, M.D., PH.D., research assistant, Institute of Psychiatry. London: Chapman & Hall (for the Institute of Psychiatry). 1957. Pp. 144. 25*s*.

THE research recorded here (in the Maudsley Monograph series) concerned the application of a variety of tests to a group of 106 normals, 20 neurotic, and 20 psychotic voluntary patients at the Maudsley Hospital. The tests included dark vision, visual acuity, accommodation, binocular vision, and retinal rivalry, as well as more complex tests, such as peripheral span, visual illusions, and duration of after-images. Many of them differentiated between groups at a high level of significance. Questionaries and other paper-and-pencil tests gave similar results. Physiological measures showed no substantial differentiation, but motor responses had a discriminatory efficiency only slightly inferior to the perceptual tests.

Many of the average differences between groups, though significant statistically, had large variances which implied considerable overlapping of scores. It would have been useful, therefore, if indices of "misclassification" had been given.

2. Puckle, O. S. Time Bases. London, 1951.

The authors seem to realise that they have done little more than apply a large number of tests to their subjects; indeed the book's title is hardly justified, for it tells us little about perceptual processes or even mental illness. In practice, it is not difficult to devise measures for discriminating between different groups on the basis of test scores, but the practical value of doing so is doubtful. Moreover, the authors' view that such tests may become important in "screening" *potential* neurotics and psychotics is based on the questionable assumption that the potentially abnormal have the same measurable abnormalities as the actually abnormal. They indicate that one limitation of their study was that the conditions for maximising or minimising the observed differences—i.e., the essential stimulus variables—could not be specified, nor could the type of population required to produce varying degrees of differentiation be predicted. Thus, with no clear identification of the main factors, theoretical implications become uncertain. The book gives a useful account of the relevant literature.

Modern Therapy in Neurology

Editor: FRANCIS M. FORSTER, M.D., dean and professor of neurology, Georgetown University School of Medicine, Washington, D.C. London: Henry Kimpton. 1957. Pp. 792. 90*s*.

ANYONE who is old-fashioned enough to regard neurology as a diagnostic rather than a therapeutic specialty, may be surprised by this sizeable book on therapy. Written by a number of American neurologists, it gives a detailed guide to treatment which would be difficult to find in any other single book. Diagnosis is discussed only when it is necessary to do so to make treatment clear.

Among the outstanding chapters is that on the treatment of myasthenia gravis. It deals with all aspects of the care of patients with this disease, describes the clinical indications for the principal drugs used in this condition—neostigmine, pyridostigmine, and 'Tensilon'—and gives an excellent account of the treatment of myasthenic crisis and cholinergic crisis. The description of how to deal with a crisis after thymectomy is especially valuable. Rehabilitation in neurological disease is wisely given a separate chapter, and so is the treatment of headache.

Clinical Management of Varicose Veins (2nd ed. London: Cassell. 1957. Pp. 169. 45*s*.).—In Prof. D. W. Barrow's concise book he draws on his extensive experience and attempts to outline the most useful methods of diagnosis and treatment of varicose veins in the leg. In the early chapters on anatomy, physiology, and pathology he flirts with an attractive over-simplification, and in the chapters dealing with examination and treatment he is firmly wed to this principle. But complications are inevitable, and in the management of the more difficult of these he becomes widely divorced from his original principle. The line drawings are very instructive and informative, but the communicating veins are always shown as short and straight and nearly horizontal, a state of affairs which bears little relation to human anatomy. Professor Barrow does not distinguish between direct and indirect communicating veins nor does he explain the main difficulties and fallacies when diagnosis depends on the so-called tourniquet test. He is a strong advocate of ligation and stripping, but he has no convincing arguments against retrograde injection, nor does he emphasise the necessity for dealing with incompetent indirect communicating veins as a separate procedure. Not all would agree with his advocacy of immediate ligation in acute thrombophlebitis, and few British surgeons would accept his extremely radical and complicated surgical treatment of the post-phlebitic limb. The bibliography refers mainly to American and Continental literature, and there are few references to British contributions. For the beginner in varicose-vein surgery, this book is a useful starting-point and a convenient guide—provided he reads it a little critically.

The Medical Annual (Bristol: John Wright & Sons. 1957. Pp. 540. 38*s*. 6*d*.).—The editors, Sir Henry Tidy and Prof. R. Milnes Walker, are to be congratulated on maintaining the excellent standard of this popular work, now in its 75th year. The list of new drugs, appliances, and books is useful, but the main bulk consists of critical reviews of recent publications, each by an expert. There is a special article on the modern views of blood-coagulation, which will attract many readers whose knowledge in this complex field is rusty.

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THE LANCET
LONDON: SATURDAY, SEPT. 21, 1957

The Function of the Gene

ONE of the central problems in genetics is concerned with how genes act. What is the function of the gene in the normal organism? How do abnormal genes produce their particular effects? Studies by INGRAM [1 2] on the chemical difference between sickle-cell hæmoglobin and normal hæmoglobin are likely to prove of fundamental significance in this connection.

The formation of sickle-cell hæmoglobin is determined by a single abnormal gene. This was established in 1949 as a result of the work of PAULING and his colleagues [3] on the biochemical basis, and of NEEL [4] on the genetic basis, of the sickling phenomenon, in patients with sickle-cell anæmia, and in clinically normal people with the sickle-cell trait. PAULING'S group found that the red cells of patients with sickle-cell anæmia contained an abnormal type of hæmoglobin which was electrophoretically different from normal hæmoglobin. In the sickle-cell trait, a mixture of normal adult hæmoglobin and sickle-cell hæmoglobin was present. NEEL showed that patients with sickle-cell anæmia were homozygous for an abnormal gene, which in heterozygotes resulted in the sickle-cell trait. It could be concluded that the abnormal gene identified by NEEL was more or less directly responsible for some peculiarity in the biosynthesis of hæmoglobin which resulted in the formation of an unusual molecule with a different isoelectric point. The normal equivalent or allele of this gene was presumably necessary for normal hæmoglobin synthesis to take place. In heterozygotes—that is, people with one abnormal gene derived from one parent, and its normal allele derived from the other—both lines of biosynthesis evidently occur and two distinct molecular species of hæmoglobin are formed. This was the first clear example of a single gene difference in a species leading to a specific peculiarity in the biosynthesis of a particular protein, with the production of an unusual type of molecule. It was to be expected that, if the nature of this peculiarity in biosynthesis could be determined, much light would be thrown on the nature of gene action. The first essential was to discover in what way the molecular structure of sickle-cell hæmoglobin differed from that of normal hæmoglobin.

1. Ingram, V. M. *Nature, Lond.* 1956, **178**, 792.
2. Ingram, V. M. *Ibid*, 1957, **180**, 326.
3. Pauling, L., Itano, H. A., Singer, S. J., Wells, I. C. *Science*, 1949, **110**, 543.
4. Neel, J. V. *Ibid*, p. 64.

It was soon shown that the difference lay in the globin moiety of the molecule, and not in the hæm.[3 5] It was also found that, apart from the difference in electrophoretic properties, the two hæmoglobins were remarkably different in solubilities when deoxygenated.[6 7] This indeed is the immediate cause of the sickling phenomenon, because sickle-cell hæmoglobin tends to come out of free solution at low oxygen tensions and produces the characteristic deformation of the red cells which contain it. But it rapidly became clear that the rather striking differences in electrophoretic mobility and in solubility must depend on very small and extremely subtle differences in molecular structure. X-ray diagrams [6 7] obtained from crystals of the two hæmoglobins seemed to be identical in every detail, and straightforward amino-acid analyses [8 9] failed to reveal any very obvious differences in amino-acid composition. Similarly no differences could be found when the N terminal residues,[10] C terminal residues,[11] or other molecular characteristics were examined. A specific chemical difference between the two globins was eventually demonstrated about a year ago by INGRAM,[1] who examined the peptides produced by hydrolysis of the proteins with trypsin. Trypsin attacks only those peptide bonds which are derived from the carboxyl groups of lysine and arginine. There are about sixty of these in both the normal and the sickle-cell hæmoglobin molecule, but since each is composed of two identical half-molecules the number of peptides obtained by trypsin hydrolysis was about thirty in each case, with an average chain-length of ten amino-acids. The peptides were separated by an ingenious combination of paper electrophoresis and paper chromatography. The great majority of these peptides in preparations from the two different hæmoglobins behaved identically. But there was one peptide spot in the sickle-cell-hæmoglobin digest which was not present in the normal hæmoglobin digest, and similarly one peptide spot in the normal-hæmoglobin digest which was not present in the sickle-cell-hæmoglobin digest. This showed that the difference between the two hæmoglobins must lie in one small portion of their polypeptide chains. INGRAM [2] has now taken this result even further. He has isolated the two anomalous peptides and determined their amino-acid sequences. The only difference between them is that the sequence in the sickle-cell-hæmoglobin peptide contains a valine residue in a situation which is occupied in the normal-hæmoglobin-peptide sequence by a glutamic-acid residue.

Hæmoglobin has a molecular weight of about 67,000. It is composed of two identical half-molecules, each containing nearly three hundred amino-acid residues. INGRAM concludes that the difference between normal hæmoglobin and sickle-cell hæmoglobin is simply that one of these amino-acid residues is replaced by another. In all other respects the molecules are the same. Glutamic acid contains a carboxyl

5. Havinga, E., Itano, H. A. *Proc. nat. Acad. Sci., Wash.* 1953, **39**, 65.
6. Perutz, M. F., Mitchison, J. M. *Nature, Lond.* 1950, **166**, 677.
7. Perutz, M. F., Liquori, A. M., Eirich, F. *Ibid*, 1951, **167**, 929.
8. Schroeder, W. A., Kay, L. M., Wells, I. C. *J. biol. Chem.* 1950, **187**, 221.
9. Huisman, T. H. J., Jonxis, J. H. P., van der Schaaf, P. C. *Nature, Lond.* 1955, **175**, 902.
10. Huisman, T. H. J., Drinkwaard, H. *Biochim. biophys. Acta*, 1956, **20**, 400.
11. Hommes, F. A., Santema-Drinkwaard, J., Huisman, T. H. J. *Ibid*, p. 564.

group not present in valine, and this is sufficient to account for the difference in electrophoretic properties of the two molecules. Presumably it also accounts for the difference in solubilities, and hence for the diverse clinical consequences in sickle-cell anæmia. The result is remarkable for its simplicity. A single gene difference such as that between the sickle-cell gene and its normal allele is presumably the result of a single mutational step. This is the smallest unit of inherited variation. It evidently leads to the smallest unit of structural difference in the hæmoglobin formed—the substitution of a single amino-acid residue. Now a gene is composed of desoxyribosenucleic acid (D.N.A.) combined with protein in a way which is still imperfectly understood. It is currently believed that the structural organisation of the D.N.A. determines the functional specificity of the gene. On the basis of the structure of D.N.A. proposed by WATSON and CRICK,[12] it is thought that the genetic information is, as it were, coded by the particular sequence of alternative pairs of purine and pyrimidine bases arranged along the length of the D.N.A. molecule. A single mutation presumably involves an alteration at some point in the character of the base-pair sequence. It is beginning to look as if the sequence of base pairs that go to make up any one gene can determine the order of incorporation of amino-acids into a particular polypeptide chain, and that a specific change in this sequence can result in a single difference in amino-acid incorporation. This may turn out to be quite a general principle. If so it will have widespread implications. For example, the manifestations of many inherited diseases can often be traced back to a defect in a single enzymic process. The affected individuals lack a certain kind of enzyme activity which is present in other people, and in general this loss of specific enzyme activity is determined by a single gene-difference. Enzymes are proteins, but they are usually present in such small amounts that they can be detected only by virtue of their catalytic activity. The absence of a particular kind of enzyme activity may be due, not to a total failure in the formation of the particular protein, but to the formation of a protein which is slightly different in structure and in consequence lacks the enzymic properties of its normal equivalent. Conceivably the absence of a particular enzyme activity, and the various metabolic and clinical consequences that result from this, could be due to the substitution of a single amino-acid residue in the enzyme protein, in a manner analogous to what seems to happen in sickle-cell disease.

Ultimately we might hope to be able to express a given individual's metabolic constitution in terms of the fine differences in the structures of his proteins, and the genetic basis of this in terms of subtle differences in the sequence of base pairs in his D.N.A.; but much remains to be sorted out. We have as yet no clear idea of how the D.N.A. structural code can be translated into the amino-acid sequence of a polypeptide. Possibly ribosenucleic acid plays an important intermediary part in this. Nevertheless, the possibility has been opened up of discussing inherited differences in molecular terms, and more particularly in terms of very simple differences in the structure of macromolecules. This is likely to prove an important landmark in biochemistry, genetics, and medicine.

12. Watson, J. D., Crick, F. H. C. *Nature, Lond.* 1953, **171**, 737.

Stones in the Common Duct

A FEW years ago some of the most eminent abdominal surgeons in the United States and in this country embarked on a vigorous campaign to establish choledochotomy as a routine part of operations for gall-stones. They maintained that the number of common-duct stones discovered would rise in direct proportion to the number of common ducts explored. They deplored the folly of getting rid of the site of origin of stones without retrieving those that had already escaped; and they looked forward to the time when second, third, and fourth operations for overlooked calculi would be part of surgical mythology rather than of surgical practice. Several well-documented series support the first part of their thesis. MCKITTRICK and WILSON[1] performed choledochotomy on 100 consecutive patients and recovered stones from the common ducts of 52. CATTELL'S group[2] reported 1104 cases; they explored the common duct in 45·7% and found stones in 16·8%. GLENN,[3] who reviewed 2472 patients, reported that choledochotomy had been performed in 10·5% and that stones had been present in a bare 7·2%. The significance of these findings, however, is far from clear. When GLENN followed up 100 consecutive patients who had had their gall-bladders removed ten years earlier without common-duct exploration, he found that in only 7 had symptoms subsequently developed, leading to re-exploration, and that in only 4 had stones been actually found. If this 4% is added to the 7·2% of his entire series, the composite 11·2% prevalence of common-duct stones is still below CATTELL'S 16·8%, and nowhere near MCKITTRICK and WILSON'S 52%. It is reasonable to suppose that stones had been present in the common ducts of many of GLENN'S patients; but that many stones had dissolved, disintegrated, passed spontaneously, or remained dormant and, presumably, harmless. That none of these fates is uncommon is suggested by clinical experience; and it is supported by cholangiographic findings.[4] Moreover, it is now abundantly clear that the gall-bladder is by no means the sole progenitor of gall-stones. Stones form readily in any part of the biliary tree; and removal of one part does nothing to discourage the process in others.

Surgeons still refer to common-duct stones discovered postoperatively as "residual," "retained," or "overlooked"; but the grounds for their gratuitous *peccavi* are often exceedingly dubious. Nobody disputes that overlooked stones exist. HICKAM et al.[5] found them ten times more often after operations by inexperienced than by experienced surgeons, and especially often when the operation had been done for acute cholecystitis, in the presence of pancreatitis or hepatic stones, or when the patient's poor general condition had compelled even the experts to limit the extent of operation. (Indeed, the danger of overlooked stones is a powerful argument against operating routinely in the acute phase of the illness.) But a prima-facie case can be made against the surgeon only when the symptoms recur immediately or soon after the cholecystectomy. This, in fact, happens rarely.

1. McKittrick, L. S., Wilson, N. J. *Calif. Med.* 1949, **71**, 132.
2. Cattell, R. B. *Surg. Clin. N. Amer.* 1948, **28**, 659.
3. Glenn, F. *Surg. Gynec. Obstet.* 1952, **95**, 431.
4. Johnston, E. V., Waugh, J. M., Good, C. A. *Ann. Surg.* 1954, **139**, 293.
5. Hickam, N. F., McAllister, A. J., Call, D. W. *Arch. Surg., Chicago*, 1954, **68**, 643.

Sometimes there is a delay of several years; there is often a silent interval of many months; and at least 80% of the patients who eventually come to a second operation leave hospital apparently cured after the first. There is still scope for improvement in pre-operative and operative diagnosis (and cholangiography gives fair promise). There is always room for perfecting surgical technique. Yet the sombre fact remains that, however skilfully the surgeon wields his probe, scalpel, or syringe, he can do nothing to safeguard his patient against recurrent stone-formation with the possible recurrence of symptoms.

SMITH et al.[6] have analysed the results of 1381 initial operations for gall-stones, performed over a nine-year period in Los Angeles hospitals. On the commonly accepted indications for choledochotomy—palpable stones, abnormal ducts, abnormal bile, a history of jaundice and pain—225 of their patients had had their common ducts opened. In the whole series there were 24 cases (2%) of retained or recurrent stones. Only 9 (1%) of these were in the group who had *not* had a choledochotomy; and of the 15 (7%) recurrences after common-duct exploration, 14 were in patients in whom at exploration stones had been found. This gave a recurrence-rate of 11% after choledocholithotomy. SMITH et al. concluded that "if the surgeon adheres to accepted indications [for choledochotomy] his chances of leaving stones behind in the unexplored common ducts are gratifyingly low"; but patients who already harbour stones in their ducts (even though all may be removed at the time of operation) "possess a source of potentially serious difficulty." Many factors contribute to the bleakness of their outlook. STERLING[7] found, in a composite series, that while the operative mortality was 0·8% after simple cholecystectomy, and 1·9% after combined cholecystectomy and choledochotomy, the mortality after re-exploration was 3·6%. BARTLETT and QUINBY,[8] in a review of 96 secondary operations performed at the Massachusetts General Hospital, reported no death: but they warned that this "does not mean that . . . the risk is negligible." HUGHES[9] recommended great caution before re-exploration, not only because of the increased mortality and morbidity, but also because of the relatively large number of patients who remained unrelieved even by two operations. Such a dismal state of affairs should not surprise us. Surgeons abandoned cholecystolithotomy in favour of cholecystectomy many years ago, because they realised that the removal of stones from a diseased viscus, so long as the disease itself could not be treated, would always be followed by the appearance of new calculi. Only wishful thinking could persuade us that this happens only in the gall-bladder. It is bad enough, on first principles, to have to remove this potentially useful organ merely because it contains a few stones; but good results justify the operation in practice. An equivalent procedure, however, is impossible when stones lodge in the common duct.

Unfortunately, our understanding of gall-stone formation has not advanced far beyond PARACELSUS's view that they are "impurities of the biliary system." We no longer, in MOYNIHAN's sonorous phrase,[10] look on them as "tombstones of dead bacteria," though the words still reverberate through undergraduate textbooks. Most of the early work on cholesterol metabolism to which NAUNYN pinned his faith[11]—he thought that excessive amounts of this substance were secreted by the inflamed gall-bladder—has been disproved. ASCHOFF's metabolic theory[12] helps to explain the origin of the cholesterol solitaire, but hardly the genesis of the far more common multiple mixed stones. STERLING[13] suggested that the "trigger mechanism" for their formation was an agglutination (antigen-antibody) reaction; but experimental proof is lacking. DRURY et al.[14] attached more importance to the pH of bile; but, though it is possible that failure of the gall-bladder to acidify liver-bile favours the precipitation of calcium carbonate niduses, their hypothesis rests almost exclusively on animal experiments. Despite the uncertainty which still surrounds their origin, much work has been done in recent years to try to deal with residual gall-stones by chemical rather than by surgical means.[15–17] BEST et al.,[15] after trying 113 different solvents, described an elaborate régime based on the instillation of chloroform and ether into the common duct through a special double-lumened T-tube. Few surgeons were able to reproduce their good results; and GLENN[18] warned against the danger of delayed cholangitis. (This grave complication has been reported even after the instillation of the far less irritating contrast media used in operative cholangiography.[19]) "It would appear," SMITH et al. remark, "that success with this (and similar) methods depends in large part upon the degree of patience exerted by the user, and also on the fortitude of the patient and his desire to avoid another operation."[6]

Investigators have been tantalised for many years by the curious phenomenon that when human gall-stones are placed in a dog's gall-bladder they dissolve or disintegrate in weeks or months.[20] ANDREWS et al.[21] suggested that changes in the bile-salt/cholesterol ratio of bile played a crucial rôle in the life-history of gall-stones; and they showed that cholesterol was precipitated when the ratio fell from the normal 20–30 : 1 below a critical level of about 13 : 1. (DOLKART et al.[22] regarded the concentration of fatty-acids rather than that of bile-salts as the essential factor.) SOBOTKA[23] later demonstrated the high bile-salt content of canine bile. On these findings, and on what they describe as the "bare possibility" that alterations in the bile-salts/cholesterol ratio might be responsible in man not only

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8. Bartlett, M. K., Quinby, W. C. jun. *New Engl. J. Med.* 1957, **256**, 11.
9. Hughes, E. S. R. *Brit. J. Surg.* 1955, **178**, 198.
10. Moynihan, B. G. A. *Ann. Surg.* 1909, **50**, 1265.
11. Naunyn, B. A Treatise on Cholelithiasis. London, 1896.
12. Aschoff, L. The Origin of Gall-Stones. New York, 1924.
13. Sterling, J. A. *Proc. Soc. exp. Biol., N.Y.* 1935, **33**, 251.
14. Drury, D. R., McMaster, P. D., Rous, P. *J. exp. Med.* 1924, **39**, 403.
15. Best, R. R., Rasmussen, J. A., Wilson, C. E. *Arch. Surg., Chicago*, 1953, **67**, 839.
16. Pribram, B. O. C. *Surgery*, 1947, **22**, 806.
17. Singleton, A. O., Coleman, J. L. *Ann. Surg.* 1956, **143**, 619.
18. Glenn, F. *In* Christopher's Textbook of Surgery. Edited by L. Davis. Philadelphia, 1956.
19. Martensson. *Acta chir. scand.* 1946, **94**, 1.
20. Best, C. H., Taylor, N. B. The Physiological Basis of Medical Practice. London, 1950.
21. Andrews, E., Dostal, L. E., Goff, M., Hrdina, L. *Ann. Surg.* 1932, **96**, 615.
22. Dolkart, R. E., Jones, K. K., Brown, C. F. G. *Arch. intern. Med.* 1938, **62**, 618.
23. Sobotka, H. Physiological Chemistry of the Bile. Baltimore, 1937.

for the precipitation but also for the occasional dissolution of stones, COLE and HARRIDGE [24] have based a new therapeutic approach. Over the past seven years they have treated 9 patients with residual stones in their common ducts (demonstrated on cholangiograms) by protracted clamping of the T-tubes and the oral administration of bile-salts 3–4 g. daily. In 7 of the 9 patients, the stone-shadows vanished within eight to thirteen weeks. Before drawing conclusions the authors wisely make several reservations. First, they had no absolute proof that the X-ray shadows did, in fact, represent calculi. In all patients the deformity was observed in more than one film. They "fulfilled the roentgenographic requirements of stones" (COLE and HARRIDGE regard the irregular shape and a surface completely surrounded by the contrast medium as suggestive, and concavity at the terminal end of the shadow as "fairly conclusive"). There was also clinical evidence that all their patients had harboured stones in their common ducts at some time; and both patients who eventually had to be re-explored were found to have them. Secondly, it could not be proved that the stone-shadows disappeared as a result of bile-salt therapy—nor could it be settled whether they had disintegrated, dissolved, or been passed. Yet COLE and HARRIDGE were sufficiently impressed to say that they "will continue to give this treatment in all [similar] cases until [they have] evidence to the contrary." Lastly this régime is obviously inapplicable to patients with complete obstruction. For the bile-salt therapy to be effective, bile must flow freely around the stones, and it must be possible to clamp the T-tube for long periods.

So many unknown factors—and some important reservations—may seem discouraging; but, whatever its shortcomings, this method marks a welcome physiological approach to an old and difficult problem. The time-honoured slogan that no stone will be left unturned can hardly reassure the patient who has them in his common duct. "No stone will be left undissolved" may hold more promise.

24. Cole, W. H., Harridge, W. H. *J. Amer. med. Ass.* 1957, **164**, 238.

Annotations

MINISTERIAL WHIRLIGIG

Mr. Dennis Vosper's resignation from the post of Minister of Health, though not unexpected, is regretted not least because of its cause, and the medical profession will join his parliamentary colleagues in good wishes for his convalescence. He is succeeded by Mr. D. C. Walker-Smith, Q.C., formerly Minister of State, Board of Trade.

Mr. Walker-Smith, who is 47, is the son of Sir Jonah Walker-Smith, M.I.C.E., who was director of housing at the Ministry of Health from 1919 to 1925. He was educated at Rossall and Christ Church, Oxford, and was secretary of the Oxford Union in 1930. He graduated with first-class honours in modern history the following year and was called to the bar in 1934. He was elected to Parliament in 1945, and since 1955 has represented the east division of Hertfordshire. In 1955 he was appointed parliamentary secretary to the Board of Trade and last year economic secretary to the Treasury. He is vice-president of the Urban District Councils' Association of the British Waterworks Association. In 1954–55 he was chairman of the Conservative advisory committee on local government, and from 1951 to 1955 of the Conservative Members (1922) Committee.

Mr. J. K. Vaughan-Morgan, who as parliamentary secretary to the Ministry of Health has deputised for Mr. Vosper during his illness, has been appointed to Mr. Walker-Smith's old post at the Board of Trade, and Mr. R. H. M. Thompson becomes parliamentary secretary to the Ministry of Health.

Mr. Thompson, who is 44, was educated at Malvern College, and before the late war was in business in the East where he has travelled extensively. From 1940 to 1946 he served in the Royal Navy. He was elected to Parliament in 1950 and now sits for Croydon South. He has held appointments as assistant Government whip, lord commissioner of the Treasury, and vice-chamberlain of the Royal Household. In 1951 he was appointed a Cottonian family trustee of the British Museum.

Stability of tenure is not one of the characteristics of political appointments, and the possibility of change is often one of the attractions of the system. But the shape of government, as of so many other things, is changing; and besides the great political offices of the Secretaries of State, which have existed for centuries, there have grown up more lately the modern Ministries which carry responsibility for the administration of the services of the Welfare State—such as education, health, and pensions. In these Ministries continuity is often important. Each new Minister who is called to office has to master the often complex legislation which he has to implement; to visit, say, the schools with which he has been entrusted; and to get to know the Civil Servants in Whitehall, and the (sometimes less civil) professions outside. Time spent in this way is valuable if the knowledge and experience gained is put to use; but frequent changes of Minister can turn it at best into an extravagant use of time and effort, at worst into an excuse for inaction, nescience, and administrative ineptitude.

Lord Moran recently pointed out [1] that, in seven years as president of the Royal College of Physicians of London, Sir Russell Brain had negotiated with no fewer than six Ministers of Health. A seventh has now been appointed and at the same time the parliamentary secretary has been changed. The record of the Ministry of Education—four Ministers in six years—is almost as variegated. But education, unlike health, has at any rate the political advantage of a seat in the Cabinet.

IMPORTING POLIOMYELITIS VACCINE

THE Government's decision to buy American-made (Salk) poliomyelitis vaccine has been generally welcomed in the press. The vaccine is being imported in order to supplement the supplies of British-made vaccine, which will not suffice to meet the demand next summer. Supplies of British vaccine have been inadequate for some time, and there has been great controversy on whether American vaccine should be imported.

The debate has not been conducted wholly at the scientific level, yet even when the pros and cons are considered dispassionately it has not been easy to reach a decision. The important difference between the two vaccines is the replacement in the British vaccine of the Mahoney strain of type-1 poliomyelitis virus used in the Salk vaccine by the less virulent Brunenders strain; and the significance of this step can be appreciated from a critical and revealing account by Meier [2] of the safety-testing of poliomyelitis vaccine. Meier reviews the background of the development of the vaccine in the U.S.A. in the past three years, and he points unhesitatingly to many scientific errors and errors of judgment. The introduction of any new vaccine on a mass basis involves a finite risk that the vaccine may not be entirely safe; but with poliomyelitis, in which the overall incidence of paralysis is very low, the use of vaccine can be justified only if the risk of acquiring the disease from the vaccine itself is extremely small. After the

1. See *Lancet*, 1957, i, 794.
2. Meier, P. *Science*, 1957, **125**, 1067.

so-called Cutter incident in 1955 the U.S. Public Health Service laid down recommendations for much more stringent test procedures which have since been widely adopted. Almost all the cases in the Cutter incident were caused by the virulent type-1 Mahoney virus, and the change to the Brunenders strain in this country provided an additional safety measure. Meier shows, too, that while doubtful virus-inactivating procedures and inadequate safety-testing methods were being used in 1954 and 1955, the public was being continually assured that the vaccine was safe; and the loss of confidence which resulted from the Cutter incident has made most observers extremely cautious in judging the safety of vaccine made under the new safety regulations.

Nevertheless 100 million doses of Salk vaccine have now been given without any measurable ill effects, and it is clear that, provided the safety-test procedures are not relaxed, the risk from its use can be considered extremely small. At the moment the vaccine is believed to protect about three people in four from paralytic poliomyelitis, but the duration of the protection is not known. On balance, therefore, the decision to import vaccine seems a wise one, but unfortunately this decision was taken too late to influence the present epidemic. One of the most regrettable aspects of the story of the development of poliomyelitis vaccine is that important decisions have often been taken under the influence of the pressure of public opinion and an emotional press. A great deal would be gained if we could decide questions of this kind as much as possible on their scientific merits. But while facts and figures may be all-important in overall policy decisions, every doctor knows that individual decisions whether or not to use the vaccine will depend a great deal on personal and emotional factors. Anxious parents who feel they must try to protect their children may be little influenced by figures, and in the long run public anxiety has probably weighed more heavily than any other factor in the Government's decision.

RECURRENT PAROTID SWELLING

IT is not uncommon for patients with mumps to give a history of a previous attack. Enders [1] has found that supposed second attacks take place in 4% of cases, but he doubts whether these are all instances of infection with mumps virus. Recurrence of parotid swelling even during a single outbreak has been recorded; one French soldier is said to have had six attacks in five months, and two buglers had three relapses each. (Ogilvie [2] has reported parotid swelling in a bugler due to air in the glands.)

Recurrent parotid swelling seems to be associated usually either with allergy [3] or with infection [4]—especially, as we have pointed out,[5] with *Streptococcus viridans*—with or without obstruction of the duct. The introduction of mumps virus into Stensen's duct of an immune monkey may occasionally cause swelling of the gland within seventy two hours, and this has been noted in man.[6] This type of allergy is uncommon, the only effect of reinfection usually being a rise in antibody.

Howlett et al.[7] have now reported parotitis associated with herpangina due to Coxsackie-A virus. In their cases the glandular enlargement was associated with the characteristic lesions of herpangina on the palate and pharyngeal wall, and serological investigations ruled out mumps infection. As the Coxsackie viruses can also give rise to meningoencephalitis and orchitis,[8] it seems that infection with them can simulate mumps. With the present improved facilities for the diagnosis of virus diseases in most parts of this country, investigation of recurrent or sporadic "mumps" might yield interesting results.

1. Enders, J. F. *In* Viral and Rickettsial Infections of Man. Philadelphia, 1952; p. 516.
2. Ogilvie, W. H. *Lancet*, 1954, ii, 395.
3. Riley, H. D. *Sth med. J., Nashville*, 1956, **49**, 523.
4. Jones, H. E. *Arch. Dis. Childh.* 1952, **28**, 182.
5. *Lancet*, 1953, ii, 664.
6. Enders, J. F. *Trans. Coll. Phycns Philad.* 1945, **13**, 23.
7. Howlett, J. G., Somlo, F., Kalz, F. *Canad. med. Ass. J.* 1957, **77**, 5.
8. Dalldorf, G. *Annu. Rev. Microbiol.* 1955, **9**, 277.

THE FAMILY DOCTOR AND THE DEAF CHILD

THE normal child learns to speak because he hears. The child who is born severely deaf, or becomes severely deaf in the early years of life, will not acquire speech normally, and, if special training is not given early, will be dumb as well as deaf. Severe deafness is usually suspected in the first year of life, and a mother is very rarely wrong when she thinks that her child is deaf. "By nine to twelve months of age it should be possible for the expert to give a firm opinion regarding the presence or absence of hearing," says a memorandum lately issued by the Ministry of Health to general practitioners in the National Health Service. Action can, and should, be taken as soon as deafness is diagnosed, sometimes earlier than the age of nine months; and there are now several pre-school clinics where educational treatment is given.

Partial deafness tends to go unsuspected for much longer, and it is usually brought to light by defects in the child's speech. There are, indeed, certain types of partial deafness in which the defect is not noticed until the child goes to school and fails to make normal progress. Mental deficiency is often suspected in such cases. The Ministry memorandum remarks:

> "Very few children are totally deaf at birth; the majority possess remnants of 'residual' hearing, which does not regress, but will only be used if specially trained. Assisted in suitable cases by a hearing aid, many such children can be successfully taught to speak, but auditory *training to be effective must be given continually during the first three or four years of life*. The importance of early diagnosis and expert supervision . . . cannot be overemphasized. The responsibilities of the family doctor and the Medical Officer of Health in this regard are obvious."

Yet it is by no means rare for the fears of parents to be brushed aside for months or even years, until an expert opinion finally confirms them. Deafness can be diagnosed as soon as it is suspected; and training or parent-guidance can be started at any age—the sooner, the better. The future of these children depends largely on early diagnosis and educational treatment of their handicap, and the family doctor can do more than anyone else to secure this.

THE SUSPENDED HEART

VARIATIONS in the electrocardiogram with changes in the position of the heart are well known, the electrical axis [1 2] being altered by rotation of the heart around the anteroposterior anatomical axis.[3] People with long thin chests and asthenic habitus have a tendency to right axis deviation, while those with a high diaphragm and sthenic habitus tend to left axis deviation.[1] It is not easy to correlate precisely the anatomical with the electrical position of the heart, and the change in the electrical axis on changing from the recumbent to the standing posture is not necessarily that which might be expected from the change in anatomical position. Sigler [4] believed that the changes in the cardiogram with position were due to variations in conduction produced by alterations in contact of different positions of the heart with the adjacent conducting media.

The ST segment and T waves may also change with alterations in posture and position of the heart,[1 5 6]

1. Master, A. M. The Electrocardiogram and X-ray Configuration of the heart. London, 1942.
2. Goldberger, E. Unipolar Lead Electroradiography. London, 1947.
3. Hermann, G. R., Wilson, F. N. *Heart*, 1922, **9**, 91.
4. Sigler, L. B. *Amer. Heart J.* 1938, **15**, 146.
5. Holzmann, M. Clinical Electrocardiography. London, 1952.
6. Ylvasaker, L. S., Kirkland, H. B. *Amer. Heart J.* 1940, **20**, 592.

sometimes counterfeiting myocardial disease. Evans and Lloyd-Thomas [7] describe a new electrocardiographic pattern in people in whom the heart, on fluoroscopy, appeared to float high off the diaphgram as if suspended from the vascular pedicle above, while tethered by the inferior vena cava below. On deep inspiration the heart and diaphragm became separated to an unusual degree, making the left cardiophrenic angle less obtuse and uncovering the inferior vena cava on the right side. Evans and Lloyd-Thomas have adopted the term "suspended heart" for such cases, and describe the cardiographic appearances in eight men and five women aged 18–68. None had evidence of emphysema, sternal depression, or cardiac disease, though several had functional chest pain or palpitations. All were of normal habitus, eight being of slender and four of medium build. The electrocardiogram showed depression of the ST segment in leads II, III, and CR_5, and in lead III on deep inspiration, resembling the appearances of posterolateral ischæmia. Differentiation from pathological tracings was possible because in all cases the exercise-test was normal, the ST-segment and T-wave changes not being increased on effort, and because of the characteristic radiographic appearances. In no case did the cardiogram alter with position. Evans and Lloyd-Thomas suggest that the recognition of the syndrome of the suspended heart by means of radiography should prevent the incorrect diagnosis of myocardial disease in patients, with symptoms suggesting cardiac disease who have ST depression on the cardiogram.

LYMPHŒDEMA

IT is now generally accepted that primary lymphœdema is accompanied by anatomical and functional derangement of the lymphatics. This disease, usually affecting the lower limbs is commonest in women but may be noticed from birth. Kinmonth et al.[8] divide their 107 cases into 12 of lymphœdema congenita, 82 of lymphœdema præcox (i.e., onset before the age of 35), and 13 of lymphœdema tarda (i.e., onset after 35). Of these 107 patients, 18 had a family history; but only 2 could be said to have Milroy's disease—that is, congenital disease with a positive family history. 14% of cases had associated congenital lesions, such as blood-vessel abnormalities, in contrast to 7% in the "normal" population. This supports the contention that lymphœdema is a developmental abnormality. As Kinmonth et al. point out, the inability to remove tissue-fluid from the soft tissues of the leg may be due to aplasia, hypoplasia, or varicosity of the lymphatic channels. They contend that the severer the functional incapacity, the earlier the age of onset: in adults lymphœdema develops only when some such additional stress as pregnancy or infection tips the scales.

The lymph in the dermis is collected by a delicate network of small vessels, from which it runs into valved collecting-trunks. Normally lymph-regurgitation from the deeper tissues to the skin is impossible. In 19 patients however, backflow of dye was observed either in the foot or in isolated patches up the limb in association with normal or dilated deep lymphatics.

Patients with excessive limb swelling of the "elephant-leg" type are still best treated by some variant of Charles's operation, in which the tissues are excised down to the muscles. The bared tissue is resurfaced with sheets of split skin taken by an electric dermatome from the leg. If the skin of the leg has been subjected to attacks of secondary inflammation or persistent stasis, its lymphatic network may be obliterated: in this case it is unwise to use the skin from the swollen area, and grafts of normal skin must be obtained from another site. Kinmonth et al. used intradermal injections of patent-blue to confirm dermal plexus obliteration; in skin suitable for grafting a patch of an inch or more in diameter shows at once as a blue network. In the vast majority of patients the disease is a minor handicap, with æsthetic rather than functional complications. Firm support for the lower leg during the day will often retard the development of œdema, particularly if it is conscientiously applied before the tissue swelling becomes hard and fixed.

7. Evans, W., Lloyd-Thomas, H. G. *Brit. Heart J.* 1957, **19**, 153.
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MORE ABOUT PRESCRIBING

NEVER, perhaps, have the activities of a profession been scrutinised so closely as those of medicine since the war; and now a book by J. P. Martin, of the London School of Economics, applies the science of statistics to the art of prescribing.[1] He describes the ways in which, during the various stages in the development of health services in this country, a degree of control of the quality and quantity of prescribing has been exercised, and he analyses much information collected for administrative purposes.

Remarkable differences have been apparent in both the rate and the frequency of prescribing as between different parts of the country, and in these an important and unpredictable factor has proved to be the "custom" of the locality. A doctor's habit of prescribing is compounded not only from attitude and training but also from the expectations of his patients, and the pattern of his practice is influenced by both the physical and the psychological climate in which he lives and works. Here we come to the shadowy borderland between medicine and psychology, which needs further exploration deliberately planned. Mr. Martin has made the best possible use of the information at his disposal, but it was collected for other purposes. Mortality statistics are a tenuous basis for discovering the relationship of morbidity and prescribing; and we could do with better information about self-medication without medical advice and control. There is likewise the effect of commercial advertising to consider, acting as it does on both doctor and patient; and we need fuller studies showing how far medication can be replaced by health education, advice, reassurance, and that basic psychotherapy which is so important a part of general practice.

Meanwhile in this book the medical administrator and the medical practitioner can see themselves at work, with the sociologist (who represents the community) looking over their shoulder. It is a unique source of information and should be a firm foundation for useful prospective studies.

CONGRESS OF THE MEDICAL PRESS

IN this country formal meetings of medical journalists are rare; but last week London was able to welcome 120 representatives of 90 journals in 29 countries. Their congress, held under the joint auspices of l'Union Internationale de la Presse Médicale and the British Medical Association, had the unusual advantage of being about the right size, and its excellent programme promoted useful discussion at the formal sessions as well as outside them. Admittedly many of the participants, attending as editors of special journals, are better known in other capacities; but the success of the congress under the presidency of Dr. Hugh Clegg, editor of the *British Medical Journal*, was itself almost sufficient to justify medical journalism as a vocation. It ended with a notable banquet in the hall of the British Medical Association at which Lord Cohen of Birkenhead proposed the health of the union and Dr. A. Plichet, its vice-president, responded.

1. Social Aspects of Prescribing. London: Heinemann. 1957. Pp. 180 21*s*.

Special Articles

PHYSIOLOGY OF THE NEWBORN ANIMAL*

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We have all been born, most of us have reached maturity, and some of us, alas, are approaching senility. We have all got to die, and if people are to do all these things gracefully they must make great physical and mental (Rudd 1957) adjustments to meet the changes which are inevitable in the world around them. We are here today to consider the newborn animal and its response to the exigencies of its environment—in other words its physiology.

In some respects the newborn animal has all the characteristics of its parents, but in others it is unlike them, and both the similarities and the differences have an important bearing upon its well-being. The differences in body-size are obvious, but there are many internal differences, such as in the function and relative size of the organs (McCance and Widdowson 1955), the activity of ductless glands, and the development of the enzyme-systems (Himwich and Fazekas 1941, Jones and McCance 1949), which will be mentioned later. The extracellular fluids, or, as Claude Bernard put it, *le milieu intérieur*, need a word to themselves. At birth these fluids resemble those of the adult in osmotic pressure and general composition, but their volume, relative to the volume of the cells and the weight of the body, is much greater. This has been surmised for many years on the basis of the determination of the quantity of chloride in the body, but it has become more certain since methods were developed for the determination of the volume of these fluids in living animals, including man (Flexner et al. 1947, Friis-Hansen 1954). Hitherto no function has been assigned to the large volume of the extracellular fluid in the developing organism, but work we have been doing has enabled us to make some interesting observations about expanding it still further. By adding a little too much salt to the food of babies and newborn piglets, we have produced extensive enlargement of the extracellular fluids, and some increase in their osmotic pressure (McCance and Widdowson 1957). The result, in piglets at any rate, has always been to reduce the katabolism of protein below that of a control animal given no salt, and this has been true whether or not the animals were being fed (see table I). Why expanding the extracellular fluids should reduce the katabolism of cellular protein remains to be discovered, but the fact does suggest that a large volume of fluid may have a functional value for a developing organism, for anything which reduces cellular katabolism will tend to promote growth.

TABLE I—EFFECT OF GIVING SALT TO STARVING NEWBORN PIGLETS ON THE KATABOLISM OF BODY PROTEIN

—	Given water	Given salt water		
		0·5%	0·7%	0·9%
Visible water balance (ml. per kg. per 24 hr.)	0	+108	+144	+193
Estimated volume of extracellular fluids (volume at birth = 100)	100	130	140	153
Nitrogen appearing as end-products (mg. per kg. per 24 hr.)	213	196	123	95

* A paper read at a meeting of the British Association for the Advancement of Science in Dublin on Sept. 10, 1957.

The New World

Consider for a moment the physiological upheaval of birth and the problems which face the animal in its new environment. Before birth mammals live in the dark, surrounded by fluid at a high and uniform temperature. They are provided through a piped system with all they need in the way of food, water, air, and drainage, and get on very well without having to make any use of the organs designed to provide these services after birth. But when the cord has been cut each of these organs has to come into action at the appropriate time and take over the function for which it was evolved. Furthermore, the animal now finds itself in a new world, surrounded by air, faced by the risk of cold, of infections, of partial or complete failure of its hitherto untried organs to meet its needs. Each species has its own particular problems and solves them in its own particular way, and one of the detailed interests of infant physiology is to study how the problems which face each species in a state of nature have been solved. There are, however, ways in which all newborn animals resemble each other and differ in these respects from adults, and these general principles are the basis of infant physiology.

Protein Transfer

Although infectious diarrhœa has probably killed more infants than any other single cause, the newborn infant does not as a rule succumb to any of the great killing diseases of later childhood. It is, for the time being, immune.

The basis of an adult's immunity is the reaction of its own cells to penetration of protein from an outside source. The response consists in the development of a highly specific substance, generally termed an antibody, which is capable of making the invading protein harmless. The immunity, once acquired, may be permanent, whether or not its development has been accompanied by any signs of disease. The newborn animal has not reached the physiological stage of development to react in this way, and would be at the mercy of many of the noxious organisms in its environment, were it not protected temporarily by antibodies which have been made by its mother and transferred to it ready-made. This protection lasts, or should last, until the young animal has reached a state of maturity at which it can deal with the production of its own antibodies.

Some young animals acquire their immunity before birth and others after birth, and the routes by which these protein antibodies of high molecular weight pass from mother to young are perplexingly diverse (Brambell et al. 1951, Brambell 1954, 1955–56, Brambell and Hemmings 1954). The rabbit, the guineapig, and man acquire this passive immunity before birth. Little is known about how this transference takes place in the last two species, but the path of the antibodies from the maternal to the fœtal rabbit has been mapped out by Brambell and his associates. Surprisingly enough, they do not pass through the placenta but reach the fœtus from the uterine cavity via the endodermal lining of the yolk-sac and the vitelline vessels. Antibodies made by the rabbit pass into the fœtus from the uterine cavity much more readily by this route than those made by man, the guineapig, dog, horse, or cow (Batty et al. 1954, Brambell and Hemmings 1954). In ruminants, horses, and pigs, the young are born unprotected and without any maternal antibodies in their tissues; but the colostrum of the mother contains antibodies in great quantities, and the health and survival of the newborn animal depends on them. These large protein molecules are absorbed through the cells of the gut in the first hours or days of life, and find their way thence to the lacteals and so to the larger lymphatics and the thoracic duct (Comline et al. 1951a and b, 1953), without undergoing any alteration

or destruction by the digestive enzymes on the way. In the mouse, rat, and dog, some antibodies are transferred before birth, and the route is known in rats. Transference after birth, however, is more important in these species, goes on for some time, and does not end in the rat until the twentieth day of life (Halliday and Kekwick 1957).

The discovery of the routes by which these large protein molecules reach the developing animal unchanged has tended to emphasise species-differences, but there are generalisations behind them of interest to all students of infant physiology. Their passage, for example, always seems to be across or through endodermal cells—of the yolk-sac or of the gut or both (Brambell 1954)—and antibodies are almost certainly not the only proteins which pass through these endodermal membranes (McCance, Hutchinson, Dean, and Jones 1949), though albumins seem to pass with difficulty, at any rate in the rat (Bangham and Terry 1957a). Other membranes and cells, moreover, may be permeable to proteins at the appropriate stage of development (McCarthy and McDougall 1953, Brambell and Hemmings 1954), and passage of these proteins may be highly selective at some sites, but relatively non-selective at others (Bangham and Terry 1957b, Hemmings and Oakley 1957). So far only the passage of antibodies has been studied to any great extent, but this transference of macromolecules from mother to young must be a matter of general importance to the physiology of the young animal. In one of our litters the serum-protein of a newborn piglet was 2·3 g. per 100 ml. At 40 hours it was 2·5 g. in a piglet given nothing, 2·6 g. in one given water only, 3·0 g. in one given sow's milk, and 5·3 g. in the one given sow's colostrum and milk.

Maintenance of Homœostasis

Ever since Claude Bernard enunciated his famous dictum, the constancy of the internal environment has been regarded as one of the greatest hall-marks of mammalian efficiency. The whole physiology of the adult is directed towards maintaining a constant internal temperature, blood-sugar, hydrogen-ion concentration, and plasma and extracellular-fluid volume, and (perhaps above all) a continuous supply of oxygen to its tissues. The activities of practically all the organs are integrated to these ends, and, when the system is subjected to a strain under which it breaks down, functional efficiency falls off and the prospects of survival diminish. It has been known since the work of the pioneers (Edwards 1824, 1832) that newborn animals cannot maintain the same internal stability as their parents. But they are also surprisingly indifferent to the resulting abnormalities in their body-fluids, and can survive changes in their own bodies and in the world around them which would be lethal later in life. To a large extent stability is a matter of the degree of development at birth, but for physical reasons some aspects of it are facilitated by a large size. This is one of the reasons why the newborn is at a disadvantage compared with its parents, and the smaller species of adult animals do not exhibit the same stability, in some respects, as larger animals such as the dog and man (Gellhorn 1937, Blood et al. 1946). Indeed, the mature rat and mouse make an interesting comparison with the newborn puppy and even with the newborn baby.

Response to Cold Surroundings

A small size and a large surface make the control of temperature difficult, and some animals which are born in a very undeveloped state have no control over their body-temperature but are indifferent to considerable and protracted departures from the maternal norm.

The newborn rat is poikilothermic, and its oxygen-consumption falls as it cools (Adolph 1948, Fairfield 1948). The same is true of the newborn mouse (Fitzgerald 1953). These animals, therefore, are incapable of maintaining their body-temperature when they are isolated from their mother and their littermates, but these are not their natural surroundings. Animals in a litter, huddled together in their nests with their mothers, have temperatures as near 37°C as makes no matter (Edwards 1824); if their mother does leave them for a time to get food for herself and their temperature falls, their uptake of oxygen and their rate of metabolism fall, too, and these poikilotherms can probably survive for a longer period of time without food than they could have if their temperature had been maintained at 37°C. Their weakness becomes a menace to their survival only if their mother fails to return to them with warmth and, after this has done its work, food. Puppies and kittens are almost poikilothermic at birth. They may have some small degree of temperature-control but, like rats, birds, and many other newborn creatures, they depend on the warmth of their nests and their mother for their well-being. It has been known for many years that they recover satisfactorily after an extensive fall in body-temperature, but how the fall affects their survival-time, its limits, and the cause of death, have not been fully investigated. The development of every newborn animal, be it a rat or a man, depends on the mechanisms responsible for its body-temperature not being overtaxed. The newborn pig is not poikilothermic, but its body-temperature is not so stable as that of an adult. It will survive and even grow well in a cold environment provided it is regularly fed, but its metabolism, like that of most homœotherms, is stimulated by a cold environment. Its well-being in nature is certainly facilitated by the warmth of its mother and the proximity of its littermates. If the newborn pig is not fed it can maintain its temperature reasonably well, and in a warm environment the unfed newborn pig will live comfortably on the food-supplies within its body for at least 2 days. In cold surroundings, however, the internal supplies of available carbohydrate fail much sooner. This may be due to thyroid exhaustion or a decline in adrenal activity or to many other things, but in any event the animal's blood-sugar falls rapidly, and unless glucose is administered, its body-temperature falls also, and it dies in hypoglycæmia (Morrill 1952, Goodwin 1957). The fall of temperature, due to the deficiency of metabolisable carbohydrate, may postpone death for a short time, but the beneficial effects must be small compared with those in a well-fed poikilotherm or (see later) in an animal deprived of oxygen.

The newborn baby is so much larger than the newborn rat or puppy that, if only for this reason, control of its body-temperature is much easier. It is not poikilothermic but, like the piglet, can tolerate a considerable fall of body-temperature below the normal 37°C provided the return is made within a reasonable time. One of its more insidious enemies, however, is long-continued exposure to cold (Mann and Elliott 1957). Babies born in very cold weather in homes that are inadequately heated are sometimes admitted to hospital suffering from the effects of this. By the time these babies reach the eye and the touch of an expert, they may have passed from a physiological to a pathological state, and present with some superadded infection. They always feel cold, but in spite of this they may appear surprisingly well, with red face and hands. Sometimes the external cold has made the extremities œdematous and the skin hard and white. The protracted exposure lowers their body-temperature internally and makes them apathetic and unwilling to take food, and perhaps because of this they sometimes have blood-sugars low enough to cause convulsions. They may die before or during treatment from what appears to be respiratory failure, and pulmonary hæmorrhage has often been found after death. Experiences with the newborn pig indicate that in resuscitation the administration of glucose in quite large amounts should precede the application of heat.

Control of body-temperature is not a simple process. It is not merely a question of available glucose. It

cannot take place properly before the nerve-centres in the hypothalamus are coördinated (Reynolds 1953), but there is much more in it than that, and workers in Prague have shown that the activity and responses of the thyroid gland, the breakdown of glycogen, the growth of fur and other mechanisms, all begin to participate at their appointed time. Young rats, aged 21 days, can maintain their temperature much better during a first than during a second exposure to cold (Hahn 1956a, b, c, and d, Hahn et al. 1956) and this has some parallel in clinical experience (Jonxis 1957).

Response to a Lack of Oxygen

When a baby is born, the transition from uterine to atmospheric respiration does not always go as smoothly as one could wish (*Lancet* 1957). The resistance of newborn animals to anoxæmia is, however, great (Adolph 1948), and some anaerobic metabolism may persist functionally after birth, even in man (Gonzales and Gardner 1957). The whole matter has been the subject of experiment since the time of Boyle (1672), and there are many records of healthy infants being born alive up to 20 minutes after the death of their mothers (Harvey 1651, Hellman 1953). Kittens, too, have been delivered in good shape after their mother had died of anoxæmia (Fazekas et al. 1941), and it is common knowledge that these animals are exceedingly difficult to drown. When adult dogs are suddenly deprived of oxygen, their blood-pressure, their respiration-rate, and the pH of their blood all rise within the first minute, but by about the second or third minute their blood-pressure has begun to fall rapidly, and respiration may cease. Resuscitation by supplying oxygen is generally possible while the systolic blood-pressure remains above 100 mm. Hg, even if all respiration has ceased, but the rate of fall is rapid and the difference between success and failure may be a matter of 15–20 seconds. The pH of the blood falls as death approaches, but remains within normal limits, and is usually not far from its initial level at the end. When puppies are deprived of oxygen, their blood-pressure, respiration-rate, and blood pH do not rise but all fall progressively. Gasps may be taken for 16–20 minutes and the circulation maintained at a very low level for twice this time. Puppies have been resuscitated 26 minutes after acute deprivation of oxygen when their blood-pressure had fallen to 5·2/3·7 mm. Hg and the pH of their blood to 6·5 (Swann 1953, Swann and Brucer 1949, Swann et al. 1953, 1954). Successful survival, however, and a useful life thereafter seem to depend on the ability of the newborn animal to make use of the energy derived from anaerobic glycolysis to synthesise the high-energy phosphate bonds which are required to maintain the proper structure and function of its brain (Stone et al. 1941, Himwich 1953, Čapek et al. 1956). As might have been anticipated, this resistance to oxygen-deprivation has been shown to vary with the species and the maturity of the animal at birth, but particularly with the state of development of the brain at this time. Guineapigs, for example, which are highly developed at birth, succumb much more quickly than rats in a reduced supply of oxygen (Fazekas et al. 1941), and the brain seems to be the most vulnerable organ, even in the undeveloped rat (Adolph 1948, Čapek et al. 1956).

A change-over from aerobic to anaerobic metabolism has two important consequences. In the first place, anaerobic metabolism produces less heat. This makes no difference to the body-temperature of a poikilotherm such as the newborn rat, but it tends to lower the body-temperature of others (unless they are in very warm surroundings), particularly of those with imperfect control of their body-temperature. Secondly, it calls for the rapid breakdown of body-glycogen and leads to the accumulation of acid end-products. A fall in body-temperature slows down all the chemical processes of the body—including the breakdown of glycogen and hence the accumulation of acid metabolites, either of which may be fatal. Many experiments have demonstrated the survival-value of this fall in body-temperature. Thus Fazekas et al. (1941) and Himwich (1953) found that the survival-time of day-old rats in nitrogen was raised from 20 minutes to 50 minutes by lowering their body-temperature from 34°C to 24°C (see also Adolph 1948). More recent and more extensive experiments on newborn guineapigs have shown that cooling the animals in ice-water up to the neck prolongs their life when they are made to breathe a mixture of 95% nitrogen and 5% carbon dioxide (Miller and Miller 1953, Miller 1954, Miller et al. 1954).

A reduction in the partial pressure of oxygen in respired air has been a common enough human experience since men began to mountaineer, and the effects in adults have been well investigated. It is generally recognised that there is no reduction in oxygen-consumption when the pressure of oxygen in the ambient air falls, even to the low levels met with at very high altitudes (Houston and Riley 1947, Pugh 1957). The oxygen-tension falls in the arterial blood, but a sustained increase in respiration and alveolar ventilation help to maintain the supply of oxygen to the tissues. This is true also of the adult dog (Cordier and Mayer 1935, Gorlin and Lewis 1954) and to a somewhat lesser extent of the rabbit (Hamon et al. 1935), and no doubt of most other adult mammals. The smaller mammals, however, do not react in this way (Gellhorn and Janus 1936), and the oxygen-consumption and body-temperature of mice begin to fall when the percentage of oxygen in the surrounding air is reduced to about 16% (Chevillard and Mayer 1935). The fall in body-temperature so diminishes the demands of the tissues for metabolic exchange that it greatly prolongs the survival-time of these animals (Strughold 1954), and this has repeatedly been demonstrated experimentally (Campbell 1936, 1938). It is possible that the thyroid is involved in this fall in temperature (Smith et al. 1946–48). The effects of anoxia on the brain can be mitigated by an adequate supply of circulating glucose (Gellhorn and Kessler 1942).

The human infant behaves like the adult rodents. If the oxygen in the ambient air is reduced from the normal 21% to 15%, there is only a trifling increase in ventilation-rate, and the consumption of oxygen falls by some 17% (Cross et al. 1955). Something of the same kind happens in puppies and kittens (Moore 1956a and b). Lambs are much more mature than puppies or kittens at birth, but their consumption of oxygen also falls when the oxygen-saturation of their arterial blood falls below 50% (Acheson et al. 1957, Dawes 1957). As might be expected, this fall in the consumption of oxygen leads to a fall in the rate of metabolism and body-temperature (Brodie et al. 1957).

If the survival studies on adult rodents can be transferred to the human infant, they have important implications. The fall in body-temperature which accompanies anoxæmia should be regarded as making for survival rather than the reverse, provided the baby can be successfully brought back to normal, and, for this, physiological principles suggest that a supply of glucose and the oxygenation of the tissues should precede the warming of the body.

Food, Growth and Renal Function

The kidney has repeatedly been cited in the past 15 years as a weak point in the functional make-up of the newborn animal (McCance 1950). It is perfectly true that, by suitable tests, the renal function of the newborn and very young animal can be shown to be less capable of maintaining the stability of the internal environment than that of an adult of the same species (McCance and Widdowson 1957). The rat is a particularly good example of this, for its kidney appears to be almost functionless

TABLE II—THE NITROGEN BALANCES OF NEWBORN PIGLETS WHICH WERE "FED" OR "NOT FED"

Nitrogen (mg. per kg. per 24 hr.)	Animals given	
	Milk or milk mixtures	Water
Intake	3500	0
Output	350	250
Balance	+3150	−250

as a homœostatic organ. Yet the composition and volume of the extracellular system remains within normal limits in all healthy newborn animals.

Few have realised the reality of this discrepancy between experience and experiment, but we have been worried about it for 10 years or more. If the kidney of the newborn really is so ineffective, how is homœostasis maintained? We began to search for a second mechanism which we shall now describe.

If an animal is growing, some of the material in its food is always being incorporated into its tissues and does not, therefore, present itself for excretion by the kidney. This relieves the kidney of the newborn animal of much of the work which it is called upon to do in adult life. The overwhelming importance of growth in relationship to every function of the body was recognised by Edwards (1824): "Dans la jeunesse tout paraît tendre au développement et à l'accroissement du corps." It was emphasised by Stransky and Bálint (1920) as an aspect of renal function, but facts of this kind are often not appreciated till they have been demonstrated experimentally. This we have been able to do (McCance and Widdowson 1956) (table II). Nine-tenths of the protein nitrogen in the food of a newborn piglet is incorporated into its tissue and never presents itself to the kidney for excretion as urea. The same is true to a lesser extent of the human baby. "Weak" and immature, therefore, as the kidney of the newborn may appear to be when subjected to some such test as the urea clearance or the excretion of para-amino-hippuric acid, it is fully capable of maintaining the blood-urea and creatinine within normal limits, provided growth is taking place as it should. Homœostasis in the newborn animal is maintained quite as much by its capacity for growth as by its kidneys, lungs, and other integrated organs.

The capacity for growth can be saturated only by an optimum diet, and the percentage of protein, fat, and carbohydrate, in the mother's milk has long been known to be correlated with the growth-requirements of the newborn animal (Bunge 1898). It now seems that the inorganic constituents of the diet must also be correlated with the function of the kidney and growth. The amount of calcium and phosphorus in human milk, for example, would never support the bone growth of a healthy piglet. The kidney of the newborn animal has a lower sodium-clearance than that of its mother, and a rise in the concentration of sodium chloride in the diet may not be followed by a correspondingly large rise in the rate of excretion. The piglet and the human baby are very alike in this respect. Salt may be retained in greater measure than water and, as already mentioned, lead to a rise in the concentration of sodium in the extracellular fluids and an expansion in their volume (McCance and Widdowson 1957). This breakdown in homœostasis is well tolerated by the newborn animal, and may even lead to a fall in the katabolism of protein; but it is unphysiological, and real well-being can be restored only by a return to a more physiological diet.

Conclusion

The weakness and helplessness of the newborn animal has been a constant theme with philosophers and thinkers since the world began, but how true is this? The newborn infant is a good risk on the operating-table. If one can detach one's thinking from the adult, a study of the newborn in its natural surroundings suggests that many of the signs of weakness are really marks of strength—if by strength is meant the ability to survive. In the face of cold and lack of oxygen, the instability of the internal environment may enhance the newborn's expectation of life rather than jeopardise it, but a young animal cannot stage its own "come-back"; it must be brought back. The piglet resists infections satisfactorily—if it has access to its mother's colostrum. The newborn, therefore, should be regarded as strong, provided it is left within its natural environment. It may be equally strong outside its normal environment, but only if all its physiological requirements are being met. They may, however, be met in unusual ways. Piglets a few days old will eat dry food, drink water, and grow as well in a wire cage as they do in a sty on mother's milk—but they must be kept warm (Haslett 1957). Finally homœostasis may depend on functions which have no place in adult life, but this need present no difficulty provided food, growth, and renal function are physiologically integrated. "Let the weak say, I am strong" (*Joel* III, 10).

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References continued at foot of next column

Personal Papers

MUMPS ENCEPHALITIS IN AN ELDERLY MAN

ONE morning at the end of January, 1954, my wife came into my room soon after breakfast and found me asleep in an armchair. She woke me up, and I recollected that I had gone to sleep after breakfast on the previous day.

Next morning she again found me asleep. She woke me up and said, somewhat severely, that I must not get into the habit of going to sleep after breakfast. I looked at my watch: it was 11.15 A.M., and I realised that I must have been asleep for two hours. I got up, scarcely able to keep my eyes open, and sat down at my desk. The next conscious incident was looking at the clock and finding it was 1.15 P.M. It occurred to me then that life would be strange if I was going to sleep for the rest of it. I was then in my 77th year.

For a day or two I had had a slight discomfort in my right jaw (which I ascribed, without further thought, to rubbing from a denture), and some tenderness in the right groin. I woke during the night and felt a little pain in the left jaw. The possibility of mumps, which I had not had, suddenly came to my mind. I found the testicle enlarged and tender, and a slight swelling, a little tender, behind the right ear. So I made the diagnosis of mumps and mumps encephalitis and then, apparently, fell asleep.

Next morning, on waking, I added the observations that there were no paralysis or paresis, no diplopia, no neck stiffness, and no other neurological signs. There may have been some ptosis, and I was unable to open my eyes completely for several weeks, but I was half asleep all this time. So I excluded meningitis and myelitis, and confirmed the diagnosis of pure encephalitis. At no time had I any vertigo, nystagmus, or vomiting.

I then stayed in bed for nearly five months (February to June), and for another six weeks from the second half of July.

The ordinary manifestations of mumps were very slight and rapidly subsided. Had I not been a doctor these physical signs might have been overlooked because of the predominance of sleep and headache. I was almost continuously asleep for the first six to eight weeks. I woke up spontaneously from time to time for long enough to turn over in bed. I could easily be woken but was unwilling to remain awake.

I could not even read headlines in the newspapers. The difficulty in opening the eyes gradually wore off. So far as I know, my intelligence and understanding were normal, but they were little tested and I could not maintain a conversation.

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I had headache of an unusual type—quite unlike anything I had previously experienced. I could appreciate that it was entirely within the skull and affected the entire brain, and had the impression that I could have traced the outline of the brain accurately. I felt the ache as soon as I lifted my head from the pillow. It was not severe, but within a minute or two I felt compelled to put my head down again.

For several weeks I insisted on having exactly the same midday meal: two steamed fillets of Dover sole in a little white sauce and three thin slices of bread and butter. I ate it quickly to get my head down again. For the rest of the day I had tea or milk and bread and butter.

Every morning after the first few days I woke between 7 and 8 A.M. feeling perfectly well; and indeed in a state of exhilaration. I used to jump out of bed, shave, and have a bath. I ran up and down the flat in spite of violent protests from the family and adjurations to get back to bed. It was glorious to be free of the headache. This lasted for about 40 to 45 minutes. Then the headache and sleepiness returned and I crept back to bed. The family strongly objected to this behaviour.

In June the headache and sleepiness were improving. I could read for short periods, but after half an hour or so the headache would become troublesome. Towards the end of the month I began to get up. Once I dressed and went to a committee which I was anxious not to miss, but I had to leave.

About the middle of July we went to a quiet place in the country, but this attempt at convalescence was premature and I returned home to bed for another six weeks, gradually getting up and about towards the end of August and in September. I thought that I had recovered by the end of September and resumed moderate activity; subsequently friends said that I still looked very ill at that time. I had lost 15–20 lb. in weight.

We left England in October for a trip round the world in a freighter. During January and February we had periods of two to three weeks ashore in Japan and Malaya. There was much travelling and hospitality which I stood without difficulty. We got back to England in April, and I could then resume previous activities.

I now need about an hour more sleep than previously. If I sleep more than eight hours one night, I wake up frequently the next night. If I have much less than seven and a half hours I do not feel fit the next day. I also need half an hour's sleep in the afternoon. Though I could sleep longer, this is sufficient, but if I do not get it soon after lunch I become miserable. If it is essential to be awake in the afternoon I take amphetamine sulphate 5 mg., which keeps me awake without any ill effects; but I do this only rarely.

The tendency to the special headache remained for at least another year on taking any liberties. Even now I feel the sensation occasionally if I am overtired, and have been short of sleep.

I am not aware of any abnormal diminution in intelligence or memory, or of physical activity. I have the common failing of advancing years of forgetting names and nouns which are quite familiar, but many contemporaries have the same difficulty.

A cousin of my age, whom I see two or three times a year, came to dinner with us on the evening before I diagnosed mumps. I kissed her when she arrived and left and we were together in the same rooms for several hours. About three months later my wife telephoned her, for no special reason, to ask how she was. She replied, "I have had a most remarkable illness. It began about a fortnight after I saw you. For six weeks I could not keep awake. Two specialist physicians came to see me but they could not find anything wrong and had no idea what was the cause." A "mild" attack of mumps in an elderly woman is evidently difficult to spot. But it is curious that we both had a pure encephalitis with it.

Public Health

ASIATIC INFLUENZA IN THE MIDDLE EAST

AN OUTBREAK IN A SMALL COMMUNITY

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THE outbreak involved Kuwait Oil Company employees and their families, and those of associated local contractors, living in the desert town of Ahmadi in the state of Kuwait at the head of the Persian Gulf. Ahmadi, the oil-company town 400 feet above sea level, is 27 miles by road from Kuwait town, the capital, and 7 miles from the oil port, Mina-al-Ahmadi. The hot dry climate from June to September is one of the most torrid in the world. Temperatures reach 120°F or more in July with relative humidity in the region of 20%.

The population of Ahmadi, numbering about 17,000, is made up of Americans, Arabs, British, Indians, Iranis, and Pakistanis, and their wives and families. The town, little more than ten years old, is compactly planned and covers about 3 square miles. Employees and their dependants live in modern brick or prefabricated houses grouped in three adjoining housing areas—Arab, American and British, and Indian and Pakistani. Most employees work at oil-company installations in Ahmadi, within walking distance of the housing area. About a quarter of the labour force is employed in Mina. Small numbers work in Kuwait town and at various outlying field sites. Labour transport to work places outside Ahmadi is by bus. Most labour employees take a midday meal in company canteens at work sites. Public amenities used at this time of the year are clubs, swimming-pools, and outdoor cinemas. Although there is a good road between Ahmadi and Kuwait town, few employees leave Ahmadi except at weekends. Throughout the summer, Indian and Pakistani employees returning from leave in India and Pakistan disembark at Kuwait.

PREPARATIONS

The medical and lay press had given ample warning of the approaching pandemic, so that preparations could be made. Colleagues in Bombay had given a good description of the clinical aspects, duration, course, complications, and response to treatment encountered there. Inquiries were made about the availability and efficacy of vaccine.

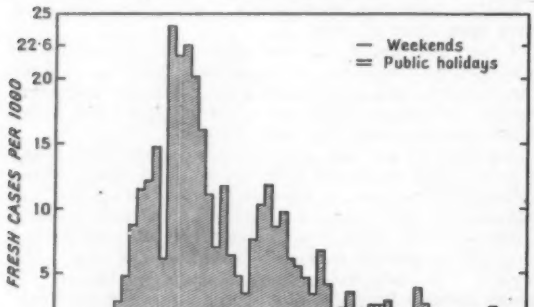


Fig. 1—Daily returns of fresh cases per 1000 labour employees.

Surveillance routines were instituted amongst employees and families returning from leave in India and Pakistan. Management was warned of the work dislocation to be expected and medical staff alerted. Medical supplies were checked and increased where necessary. Depletion of medical staff was to be expected, since doctors and nurses highly exposed to it were likely to fall prey to the illness. A number of former nursing sisters now married and living in the community volunteered to help in an emergency.

A principal cause of anxiety was the risk of heat hyperpyrexia in patients under treatment in uncooled houses in the first few days of the illness when their temperatures would be high. It seemed imperative to increase the number of hospital beds so that those with high temperatures could be admitted to cool wards, and this was done.

COURSE OF THE EPIDEMIC

The returns illustrated in fig. 1 are derived solely from the 6406 labour employees working directly for the company. There was no obvious difference between the

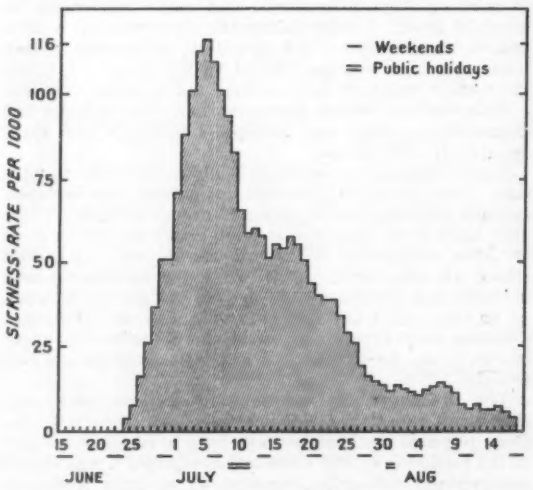


Fig. 2—Daily sickness-rates per 1000 labour employees.

incidence of infection amongst Arabs, Indians, Iranis, or Pakistanis. There was one death during this period.

The general pattern of the outbreak is clear despite distortion by weekends and by public holidays. The first sporadic cases were all Kuwaiti Arabs, but before the end of the first week patients were seen who had recently arrived by boat from Karachi (many told of small epidemics amongst the passengers en route). The figures for the third and fourth weeks of August resembled those of the second. There was another death on Aug. 22.

An apparently similar pattern was seen in the returns of illness in staff employees and their families, but the attack-rate was only about a quarter of that in the labour force. Again there was no racial variation between Americans, Arabs, Britons, Indians, and Pakistanis. The numbers are too small to record graphically.

There was no apparent difference as judged clinically or statistically (comparing the mean maximum temperature-rates recorded and the number of days off work) in the severity of the disease in staff patients and labour employees. By the same criteria there appeared to be no variation in its virulence during the course of the epidemic. Immunity was short-lived and just over 2% had a second attack, one indeed having three influenzal illnesses in the period under consideration. The shortest interval between the onset of symptoms in consecutive episodes was fourteen days. The second attacks tended

on the whole to be shorter in duration than the unmodified illness.

MORBIDITY

Fig. 2 shows the time lost through sickness as recommended by the attendant doctor amongst 6406 labour employees during the period. Time lost is included only when it is directly related to the initial illness. That caused through reinfection or complications after a period of apparent good health is not shown. Fig. 2 illustrates clearly the course of the epidemic. The two small upthrusts with their peaks on July 13 and Aug. 4 were appreciated by the medical staff as they occurred, and at the time caused apprehension. The average period of sickness of the 1990 patients was 6·9 days.

Figs. 1 and 2 were compiled from a study of 1429 case-records from Ahmadi clinic and extended to represent the actual 1990 patients with influenza in the labour force.

CLINICAL FEATURES

Outpatients

In two of the clinics, Ahmadi and Magwa, a standard questionnaire was introduced in the later stages and during the period the observers (D. M. F. and J. G.) were constant. At the third clinic in the port area no questionnaire was used and the figures were obtained from the records of three different doctors.

Typically the patient was a young male seen within twenty-four hours of becoming ill. He looked completely dejected and complained bitterly of headache, usually frontal or retro-orbital, and generalised body pains. The scleræ were usually injected. Abnormal chest signs were rarely present, despite the frequency of retrosternal pain. The throat was often characteristic—red, dry, and mat with little involvement of the fauces.

Treatment was symptomatic, patients being sent home to bed, and to take copious fluids with added salt and sugar. Penicillin, aureomycin, or 'Achromycin' were given empirically to a few patients but did not seem to alter the course of the illness.

Complications were heat syncope, bronchitis, bronchopneumonia, herpes simplex, hæmoptysis, hæmatemesis, epistaxis, and prolonged socket oozing after dental extraction in the post-influenzal period.

Inpatients

The great majority of patients admitted to hospital were Arab, Indian, or Pakistani adult males. 69% were between the ages of 20 and 35 years. Few American or British were treated in hospital.

The principal indications for admission were:

(1) High temperature (103°F and above).
(2) Presence of complications.
(3) Toxic appearance (some patients looked very ill, and were drowsy or collapsed).
(4) Severe dehydration, particularly if the patient was pyrexial.
(5) Prolonged low-grade pyrexia.

Bed rest in wards cooled to 75 to 80°F and the administration of copious cool fluids, salted if necessary, were considered the most important measures.

In general, improvement was rapid. Temperatures often fell overnight to nearly normal levels. Despite this initial fall, a low pyrexia usually persisted for three to five days (60%). 8% remained pyrexial for six days. The remainder had settled to normal limits within two days. Pulse-rates were rapid (100 to 110 in 47%, 110 to 140 in 35%) and fell in step with the temperature.

Symptoms usually cleared up as the temperature subsided though tracheitis with thick purulent sputum and retrosternal pain on coughing often persisted for a week.

Patients with bronchitis, bronchopneumonia, or segmental pneumonia were given penicillin (500,000 units b.d.), and most of them made a rapid recovery.

In 3 patients the clinical picture was sufficiently suggestive of acute appendicitis to warrant admission to a surgical ward for observation. A dry furred tongue, with abdominal pain in the umbilical area, vomiting, tenderness over McBurney's point, pyrexia, and a rapid pulse were present in 2 of these. The third had in addition, guarding of the right rectus, diarrhœa, and a palpable mass in the right iliac fossa. In the first two the symptoms disappeared within twenty-four hours, and upper respiratory symptoms, muscle pains in the limbs and back, headache, and rhinitis developed. A normal appendix was removed from the third.

5 patients (1 of them very drowsy) presented with neck rigidity, neck pain, and headache. Lumbar puncture, performed in 3 cases, revealed clear fluid under normal pressure. Examination of the C.N.S. was not remarkable apart from the neck rigidity which disappeared within forty-eight hours.

Though the medical staff had been on the alert for poliomyelitis, a patient treated for influenza subsequently reported as an outpatient a few weeks after discharge, with weakness and wasting of the scapular muscles on one side. A diagnosis of poliomyelitis was made.

Maximum *temperature* and *pulse-rate* in 350 patients admitted to hospital were as follows:

Temperature (°F)	*No. of patients*	*Temperature* (°F)	*No. of patients*
98	4	101·5 to 101·9	17
98·5 to 98·9	4	102 to 102·4	57
99 to 99·4	12	102·5 to 102·9	30
99·5 to 99·9	7	103 to 103·4	68
100 to 100·4	23	103·5 to 103·9	20
100·5 to 100·9	11	104 and above	54
101 to 101·4	38		

Pulse-rate (per min.)	*No. of patients*	*Pulse-rate (per min.)*	*No. of patients*
80/84	14	115/119	18
85/89	5	120/124	66
90/94	25	125/129	11
95/99	12	130/134	11
100/104	66	135/139	00
105/109	15	140 and over	6
110/114	69		

The *duration of fever* was:

Days		*Days*	
Less than 1	3%	4	24%
1	9%	5	18%
2	19%	6	8%
3	18%	7	1%

The *total duration of illness* was:

Days	*No. of patients*	*Days*	*No. of patients*
2	5	13	7
3	8	14	8
4	11	15	9
5	21	16	2
6	42	17	1
7	66	18	1
8	43	19	1
9	48	20	1
10	24	25	2
11	22	28	1
12	18		

The total duration of illness was six to ten days in 66% of those admitted. The stay in hospital was two to five days in 80% of those admitted.

Clinical manifestations among the 350 admitted were analysed as follows:

	No. of patients		*No. of patients*
Headache	87	Retrosternal pain	30
Backache	22	Sore throat	51
Aches and pains	108	Throat changes	30
Giddiness	5	Rhinitis	58
Vomiting	21	Cough	118
Abdominal pain	7		

Complications were:

	No. of patients		*No. of patients*
Bronchitis (clinical)	77	Otitis externa	2
Bronchopneumonia	14	Urticaria	2
Pneumonia (segmental)	16	Bleeding per rectum	1
Diarrhœa	3	Hæmoptysis	1
Herpes simplex	2	Splenomegaly	2
Neck pain or rigidity	5	Amœbiasis	1
Otitis media	2		

SPECIAL INVESTIGATIONS

Throat-washings were collected on the first day of illness, put into 20% glucose broth, packed on dry ice in a vacuum flask, and flown to England for virological investigation. Blood was also collected on the first and

fourteenth days from the same patients and the serum separated and sent for antibody investigation.

Three weeks later a further batch of throat-washings was collected and despatched, and more sera. In the second batch 4 known relapsed cases were included, since it was thought possible that mutation of the virus strain may have been the cause of the relapse rather than a rapid loss of immunity.

Results received state that both influenza A and Asian strains were isolated and there was no evidence of mutation. Results of antibody studies are not yet available.

White-cell counts.—These ranged between 3000 and 14,000 cells per c.mm. with an essentially normal differential count and blood-film. High counts were found in cases with respiratory complications, associated with neutrophil leucocytosis.

Throat swabs.—Where these were taken the normal flora were reported or predominantly a viridans streptococcus.

Cerebrospinal fluid.—Three specimens: all clear fluid under normal pressure.

Deaths

Both patients who died were middle-aged Indian males. The first died ten days after the initial onset of illness. The second, having had an influenzal attack three weeks previously, fell ill again in a similar way. He had a hæmoptysis on the first day and was admitted to hospital, where he died within twenty-four hours.

First necropsy.—Right atrial dilatation. Liver, spleen, and kidneys were congested. Trachea was intensely congested, main bronchi contained brownish frothy mucus; fibrinous exudate over the left lobe. Both lungs showed a confluent bronchopneumonia posteriorly in the lower lobes, patchily distributed anteriorly, and in the right middle lobe. Upper lobes œdematous. Other systems unremarkable.

Second necropsy.—Bilateral slightly turbid straw coloured pleural effusions of about 200 ml. Both lungs partially collapsed and extremely œdematous. Main bronchi contained hæmorrhagic watery fluid and trachea moderately injected. Other systems normal except for arteriosclerosis compatible with age.

Bacteriology.—Films from lung swabs at second necropsy: no organisms seen, scanty debris. Cultures aerobic and anaerobic, a coliform bacillus isolated (regarded as a contaminant).

The first death was considered to be due to secondary bronchopneumonia and the second to a primary influenzal pneumonia with associated pleural effusion.

COMMENT

When an epidemic of influenza is expected the disease should be made notifiable, if sufficient clerical staff is available, so that the course and direction of spread may be followed and plans may be made promptly in anticipation of work dislocation.

Before the epidemic reached Ahmadi those returning from leave in India and Pakistan had been placed on a five-day surveillance routine. This measure proved to be quite ineffective but kept the medical staff vigilant. Early in the outbreak the advisability of closing schools and other public gathering places was considered. The schools were about to break up at the end of term, and stayed open for the last few days. Cinemas and swimming-pools are all out of doors; they are, moreover, important to morale in an isolated community, and it was not recommended that they be closed.

Some weeks before the epidemic reached Ahmadi inquiries showed that vaccine could not be expected for at least a month and then in doubtful quantities. According to the information available at the time the immunity conferred would take about two weeks to develop and would last for only two to three weeks. There was therefore little point in obtaining vaccine.

The expected depletion of medical staff amounted in this outbreak to one quarter of the nursing and medical staff being incapacitated for part of the period.

The mode of entry of the infection is uncertain, but the virus was most probably carried in by employees and their families returning from India and Pakistan.

There were striking differences in attack-rate between staff and labour employees. In the latter the spread-rate was three times as great, probably due to their living more closely together, and their more intimate contact in work, buses, and canteens.

The course of the outbreak showed three peaks of declining magnitude separated by intervals of eleven to fifteen days. Reinfections were noted after a comparable period, which might represent the interval between the acquisition and loss of immunity.

Fortunately there were no cases of hyperpyrexia, and we attribute this to the policy of admitting patients with dangerously high temperatures. Cool wards and the prompt correction of dehydration were believed to be the most important reasons for the rapid improvement of almost all patients taken to hospital.

Retrosternal pain was much less common in those reporting sick at Mina-al-Ahmadi, cough was less, and pulse-rates lower. The much higher humidity in Mina may account for the first two differences, but the lower pulse-rates were surprising in conditions of high humidity.

The clinical impression that latterly the infection became milder was not borne out statistically.

We wish to thank the management of Kuwait Oil Co. Ltd. for permission to publish this article and for affording statistical facilities. We are indebted to our lay and professional colleagues for access to case-records and assistance in the preparation of this paper. The virological investigations were carried out by the Virus Research Laboratory, Colindale.

Influenza

New outbreaks of influenza continue to be reported, especially from schools, factories, and Service establishments. East Lancashire and the Midlands have been most affected; in Derbyshire over 1000 school-children, and in Bradford over 10,000, have been absent at once with influenza, and at a school in Bacup no lessons were given because every teacher was away with influenza. Weekly new claims on the Ministry of Pensions and National Insurance have been higher than for the corresponding weeks of last year, and increasing: thus during the week ended Sept. 4, new claims rose by 18,098; most of the increase was in the East and West Ridings of Yorkshire and North-Western region.

The Government has said that enough vaccine will be bought to offer protection to those at special risk, including family and hospital doctors, nurses, and public-health workers. The statement emphasises that the disease is generally mild, but some deaths have been reported: a man, aged 20, died of hæmorrhagic pneumonia following influenza six days after returning from a pilgrimage to Rome.

At a Royal Air Force Station near Hereford, where at the beginning of this week 60 men were in bed with influenza, all windows of billets and classrooms were to be left open day and night.[1] Extra blankets were issued, and airmen were allowed to attend classes in greatcoats. A vaccine was being used experimentally at a naval establishment near Ipswich, where 850 men and boys were ill with influenza. The Scottish National Blood-transfusion Service appealed to the crew of H.M.S. *Eagle* for convalescent serum for the treatment of infants with influenza,[2] of which there had been an outbreak in the ship.

Stinging Jellyfish

The arrival of Portuguese men-of-war off south coast beaches in the past three weeks must have been the final blow to holidaymakers who had already suffered much from the weather. These unpleasant stinging members of the jellyfish family are usually confined to an area between the Azores and North-West Africa, but a few are found off the Cornish coast in most years. In 1954

1. *Times*, Sept. 17, 1957.
2. *Manchester Guardian*, Sept. 6, 1957.

the "invasion" got as far as Devon and South Wales. This year the men-of-war have advanced still further along the Channel and last week they put in an appearance at Hastings and other Sussex resorts. Warning notices about the dangers of bathing or touching jellyfish on the beach have been posted in many places.

The jellyfish looks like an inflated transparent plastic bag, tinted faintly blue, with a long fringe across the dome, which can act as a sail and carry the creature where wind and tide decree. All this would be innocent enough were it not for the filaments which hang down from the floating sack for anything up to 50 or 60 feet. Some of these carry poisonous barbs which can inject a powerful neurotoxin, paralysing a fish and enabling the organism to feed on it. The toxin affects the motor muscles, particularly the respiratory groups. In man the sting is very painful, large inflamed weals are raised, and severe shock may ensue, and occasionally muscle paralysis. Rarely, death from shock has been reported. The first-aid treatment used by coastguards on American beaches is the application of household ammonia. Prompt action against shock may be needed in the severely poisoned.

Poliomyelitis

Uncorrected poliomyelitis notifications in the week ended Sept. 7 were as follows (previous week in parentheses): paralytic 158 (151), non-paralytic, 121 (156); total 279 (307). The following figures compare this year, up to and including the 36th week, with the preceding nine years.

Year	*Total cases up to and including 36th week*	*Cases in 36th week*
1948	1214	76
1949	2645	306
1950	5126	513
1951	1923	86
1952	2791	188
1953	3478	173
1954	1482	78
1955	3446	458
1956	2185	108
1957	4011	279

Medicine and the Law

Deaths after Anæsthesia

AT an inquest widely reported in the press this week the Walthamstow coroner is said to have declared to an anæsthetist: "Where 5 people have died it cannot be a case of fortune looking the other way every time." [1] The inquest was concerned with the death, after an anæsthetic, of a 6-year-old girl in Whipps Cross Hospital, and the coroner referred to the fact that the anæsthetist had been involved in 5 cases in which patients had died during or after anæsthesia. Unhappily not all the newspaper accounts of the proceedings made it clear that these 5 cases were spread over a period of seventeen years. Another ambiguity in the reports arose from a remark given during evidence by an adviser in anæsthesia to the Ministry of Health. Asked by the coroner whether he took the view that it would be an advantage if the anæsthetist concerned were to attend a postgraduate course, the adviser's reply was reported [1 2] as: "It would be advantageous to everybody." Most readers would interpret that as meaning that the adviser held the anæsthetist to be less than competent; but, conceivably, he meant that all anæsthetists (or doctors) would benefit from attending a postgraduate course from time to time. The adviser also gave his view that the respiratory failure from which the child died was probably the result of the anæsthetic solution that was injected. In none of the reports we have seen was the drug or the dose named. Recording a verdict of accidental death, the coroner suggested that the anæsthetist took a course "to keep up to date with modern drugs in anæsthetics."

1. *Daily Telegraph*, Sept. 17.
2. *Times*, Sept. 17.

In England Now

A Running Commentary by Peripatetic Correspondents

HE was a large worried-looking man. He sat down heavily, drawing his hand despairingly across his forehead. "Something troubling you?" I asked kindly. "What me, Doctor? I haven't a care in the world, nothing's ever bothered me." I politely expressed disbelief and he looked even more worried and dropped his insurance card on the floor. "It's just this little toe here. Does it look bent to you, too?"

Next was a small woman totally surrounded by children. "Of course I love children," she said, giving one a swipe that sent him howling into the corner. "It's this leg," she said, pushing a couple of children off it and into the waste-paper basket. "Come orff it," she yelled, and swam through them to seize the youngest who had started eating the coal. "Don't know what I'd do without 'em," she said as she went out dragging them by the hair.

Quite a run of these kind of patients I've had—a woman passionately devoted to a merchant-seaman husband but mysteriously racked by pains whenever he returns on shore-leave; a child devoted to its parents who gets asthma when stepfather gets drunk; a man obsessionally fond of his fiddly employment who gets blinding headaches in working hours. After watching their unconscious (although the conscious isn't always so un) chuntering away down below in the opposite direction, I start to see all sorts of denial in daily life. The butcher does it ("Best Prime Beef"), and the greengrocer ("Fresh Today"), and the coalman's unconscious must be a seething mass of complexes or complices or whatever they are, and then, blow it, what about me ("Just take this medicine before meals and you'll soon feel right"). For all the gallons of mist. morph. et ipecac. that have coursed down the alimentary canals of my patients, how much has passed down mine? Not one dose! But there; it's wonderful being a doctor, come rain or fine, hail or high water, 5% or 24%, it's wonderful to be making people *better*, relieving suffering, doing *good*. (Although even here I begin to gain a little insight after a couple of needless night calls.)

* * *

Today the first words read in any book are usually not those written by the author but those written by his publisher. Not unreasonably the style of the blurb varies. There is the enthusiastic and rather endearing "In *Pink Narcissi* Miss Carmen Bloggs has written a novel which will rank above *Gone with the Wind* and *War and Peace*"; the subtler unexpectedly denigratory "You may wonder why we have published this book; sometimes we do ourselves"; and the strictly factual "*Slug and Trowel* is the record of three years spent in a large garden in the heart of Loamshire."

The serious publisher also offers his readers useful biographical and/or explanatory notes, and Mr. Evelyn Waugh's publishers were following orthodox practice with elegance and wit when they wrote on the jacket of the *Ordeal of Gilbert Pinfold* [1]:

"Three years ago Mr. Evelyn Waugh had the disconcerting experience of suffering from a brief attack of hallucinations. He later learned that this was not nearly as rare as he supposed. It is a state of particular interest to a narrative writer. The reason remains strenuously active but the information on which it acts is delusory.

"Recollecting these emotions in tranquillity, Mr. Waugh has made them the theme of a light novel which should delight all those who live on the border lines of sanity—rather more than half the inhabitants of the kingdom according to medical figures."

Following Wordsworth's instructions, writers have for years been recollecting emotion in what tranquillity they can muster. But if they are writing a novel it is doubtful how wise it is for them (or their publishers) to take their readers into their confidence. When I am reading, say, about Mr. Huxley's reactions to mescaline, any facts that I may have picked up before opening the book about his experiments with the drug add to my appreciation of the contents. But when I am reading about Mr. Pinfold's unhappy experiences I confess I find it only

1. London: Chapman & Hall. 1957. Pp. 184. 12*s*. 6*d*.

distracting to know that Mr. Waugh has also suffered from hallucinations.

Furthermore, the reviewers, no doubt inflamed by the hint in the blurb, in each of their well-balanced and discriminating reviews, informed those of us who were unaware of Mr. Waugh's private circumstances that the resemblance did not stop at the little mâtter of hallucinations. Mr. Pinfold, like Mr. Waugh, is a writer and a Catholic convert who lives in a large country house with a much younger wife and large family of young children. With so much similarity I found it difficult to get Mr. Waugh out from under my feet so that I could concentrate on poor Mr. Pinfold and his troubles. How much of this, I kept asking myself, was recollected in how much tranquillity? Moreover I felt guilty about the whole thing. My curiosity was surely ill-bred, prying: Mr. Waugh's affairs were no affair of mine. Yet it was surely unfair to expect me to ignore the entire connection between the two when I had been told so much about it.

It says a great deal for Mr. Waugh's pen that despite these distractions he conveyed to me so clearly the nightmare, frustrated, unhappy, feelings of Mr. Pinfold. But the hallucinations themselves seemed to me less convincing than the feelings they aroused. And here again I found my knowledge of Mr. Waugh's private life disturbing. Were the hallucinations less convincing, and more amusing, because Mr. Waugh had substituted symbolic, significant, communal hallucinations for his personal and private ones? Mr. Waugh again had come between me and Mr. Pinfold, and I closed the book with a sigh. Writing it no doubt had cured Mr. Waugh; but what about Mr. Pinfold—and indeed by this time me?

* * *

As he was dreamily inducing, the slow-speaking anæsthetist said, "This child has got a hacking cough," and then in a more contemplative tone he murmured, "I wonder why its called a hacking cough." The surgeon, rationally minded as ever, said brusquely, "Well, it must be something to do with horses, like a hacking jacket." "Oh," drawled the anæsthetist, "I understand now. You mean the cough is due to bucking bronchos."

* * *

If there's one thing that goes down well it is a cup of tea in the morning. Don't know how I'd face breakfast without it, let alone the morning surgery. My wife agrees, so the early morning cuppa has long taken a prominent and indispensable place in our little home. Thus it was that not long ago the wifely eye caught sight of a gadget in the window of our local electrician, who seems to hear of these things just five years after everyone else. Bang went a sum equivalent to mileage from here to Vladivostock, and so 'Teazupp' came to stay at our bedside. A crafty little device, it wakes you up, pours you out a cup of ready-made tea, and turns on the light. For a small extra charge it will turn on the wireless or recite the first stanza of *Omar Khayyám*.

The ritual starts in the evening: a large tray is laid with cups and saucers and things, tea is poured in one orifice and water in another, various little levers and knobs are adjusted, and so to bed. Your wife then starts remembering things. You go down for the milk, which you fetch just in time to return for the tea-strainer. You check the mechanisms again, and by this time you feel you need a cup of tea. Come the morning, and the fiend emits hissings and rumblings a good ten minutes before it finally explodes upon the world with a newborn cup of tea. You stretch out an ataxic groping hand to find that an inadvertent jog at some stage has sent the boiling water all over the traycloth and last week's *Lancet*. And the milk's gone sour.

We have a better system now. There's an alarm clock that doesn't pretend to do anything except wake you up. My all-round multilateral general-purpose wife then gets up and puts a kettle on the gas-ring. Within 3 minutes the tea is ready: no fuss, no bother, no late-night fumblings. So if any reader would be interested in purchasing a quite serviceable and only slightly dented little device . . . ?

* * *

"Worrying about myself has got on my nerves, doctor."

* * *

From the doctor's postbag.—"You gave me an injection in my face as I was suffering from Tic-de-la-rue." Doubtless the result of walking down a draughty street.

Letters to the Editor

FAINTING AND CEREBRAL DAMAGE

SIR,—Dr. Bourne's thought-provoking article in your last issue provides a worthy milestone not only for the dentist but for every abdominal surgeon. Assuredly it emphasises the teaching and research of Spalding,[1] Ogilvie,[2] and Brock[3] at Guy's more than a decade ago, teaching which still is perhaps not so constantly practised as it should be—namely, to abstain postoperatively from the Fowler position. Dr. Bourne's work is a real landmark, giving us explicit physiological explanation for those deaths and complications due to unexplained ileus, cerebral hypoxia, and so-called postoperative shock. Surely then it is time that we all became anti-Fowlerites or anti-sitters-up, before, during, and after anæsthesia, for any purpose.

London, W.1. V. B. GREEN-ARMYTAGE.

SIR,—With great respect to Dr. Bourne for his excellently documented and authoritative article, and without any question of disagreement, I suggest that his splendid sermon ex cathedra fails to descend from the pulpit and get among the wrapt congregation in the pews.

There are, for instance, frequent references to insufficient oxygen during dental anæsthesia, but no suggestion of what he considers to be the ideal quantum. It is as if an archbishop were dilating upon the ideals of theology without reference to practical means of achieving them. Possibly the experience of over a third of a century of dental (and other) anæsthetics, during which I have given many thousands, may prove of some interest, possibly of sufficient weight to induce Dr. Bourne to give us the practical results of his great experience.

In these days of continual nasal anæsthesia for dental operations I feel that it is wrong for dental surgeons to give their own anæsthetics, not by reason of any lack of expertise, but because they cannot give their whole attention to the anæsthetic. They can do little more than give a deep induction and hope for the best.

In the old days of nitrous oxide alone we had to give as deep an anæsthesia as possible, which always produced some degree of hypoxia, and reinduction was a hazardous business. But, with modern nitrous-oxide-plus-oxygen apparatus, prolonged anæsthesia, or preferably analgesia, is infinitely safer.

In almost a lifetime of this work I have come across only two cases of unusual difficulty, which are worthy of note.

A man, aged 42, had had three cerebral operations, and he became deeply cyanosed even before consciousness was lost, with extremely heavy oxygenation. I gave him three dental anæsthetics in all and, despite the administration of almost pure oxygen in each instance, the reaction was the same. This poses a pretty pathological problem which I cannot attempt to solve. He suffered no ill effects.

A boy of 6 years, who screamed and fought (which is in my experience extremely unusual in young children), was not really anæsthetised at all. Only one tooth had to be extracted and, while he was still screaming, I told the dentist to go ahead because the child was sufficiently analgesic not to feel the extraction.

Fifteen seconds after the extraction he suddenly became white, pulseless, and apparently dead. No oxygen was then given but he was upended and artificial respiration was given for 25 minutes. He recovered completely, was quiet and subdued, and told his father that he had "felt nothing." While one cannot put down such a phenomenon to anoxia, I suggest that the child falls into a rare category, not mentioned in Dr. Bourne's article, of a gross psychosomatic syndrome.

1. Spalding, J. E. *Lancet*, 1946, i, 643.
2. Ogilvie, W. H. *Ibid*, p. 715.
3. Brock, R. C. *Proc. R. Soc. Med.* 1956, **49**, 347.

In the first case quoted by Dr. Bourne, is it not possible that pulling a child up in the dental chair " by its head " may have had something to do with the sequel ? May not pressure on the carotid sinus have been responsible? This is not so far-fetched as it seems. I have a patient whose heart invariably stops when the left carotid sinus is compressed. A few weeks ago this girl " passed out " and was comatose for over half an hour because her hairdresser, quite innocently, compressed this sinus during a " perm." Admittedly she has a carotid-jugular anastomosis (aneurysmal), but that is beside the point. It is easy enough to induce a fainting attack by pressure in this area.

As for the practical side, I find that getting the interest of young children (e.g., telling air-minded lads that the nose-piece is like that worn by airmen and it feels just like going up in a jet plane) during induction, and quiet, almost hypnotic assurance of adults in this period are of enormous assistance.

For induction, my experience is that to take them slowly through the air-gas section of the scale, during which, if any emotion is shown, one can say " You are not getting anything but plain air," followed by a quick crossing of the pure-gas segment into gas plus approximately 4% oxygen, is about the ideal.

For the rest, acute observation of colour and respiration is practically always all that is required.

Dr. Bourne says nothing about rebreathing. Am I wrong in the assertion that shallow respiration with good colour more often calls for a few breaths of rebreathing than for a surplus of oxygen ? I have always found it so, and have often wished for the addition of carbon dioxide to the anæsthetic apparatus.

I have never yet used the addition of trichlorethylene or ethyl chloride to gas, and feel that they should not be used in any but the recumbent position.

Finally, I append an experience which could have had serious consequences. I invariably ask how many teeth are to be dealt with, and the dentist, in this instance, said " only one." When the patient was lightly " under " he started on a job which took him twenty minutes ! The danger of ordinary dental anæsthesia in the usual position in a dental chair is slight ; but that danger rapidly increases with the duration of unconsciousness, and prolonged dental operations should never be done in any but the prone position.

Loughton, Essex. G. B. KIRKLAND.

SIR,—Dr. Bourne's excellent paper (Sept. 14), underlining the danger of maintaining the vertical position after fainting, recalls to mind the extraordinary photographs we see each June, at the time of the annual ceremonial parades, showing guardsmen suffering from acute cerebral anoxia being maintained in the upright position at all costs by stalwart comrades, strategically (if unphysiologically) positioned at either side.

Although I appreciate [1] how difficult it must be for the Army Medical Services to impress upon their military colleagues that the maintenance of a tidy line on parade is secondary in importance to the dangers of decerebration, it does seem, in the light of current knowledge, that some drastic rethinking is required.

London Varicose Clinic, London, S.W.11. STANLEY RIVLIN.

CONSULTANT AND SPECIALIST

SIR,—The fear that an intermediate grade between registrar and consultant would be abused—the only substantial argument against it—could be removed immediately by the perfectly just expedient of making it financially pointless to do so. There are already " intermediate " grades (some 3000 S.H.M.O.s, some G.P.-specialists, and some senior registrars) doing unsupervised specialist work. That they are being exploited is doubtless true —and to this extent they may well be called " stooges." But that they are essential to the functioning of the N.H.S. has never been in question.

Surely the answer lies in an intermediate grade with a proper status and title to include all those without consultant status at present doing unsupervised specialist work in N.H.S. hospitals. Such a grade should (1) be a necessary step towards consultant status ; (2) provide a satisfying career for those not achieving consultant status; (3) carry rates of pay which would *continue* to rise to the highest normal rate paid to consultants.

New recruitment to such a grade would be based on those standards at present associated with consultant status. The ultimate achievement of consultant rates of pay would render pointless any abuse by any authority. —and is indeed only an expression of the principle of " the rate for the job." Consultant status would continue to enjoy the added incentives of merit awards and (probably) better prospects for private practice.

Such a suggestion would I believe satisfy all except those who hold dogmatically to the belief that all specialties and all specialists are equal. It need not interfere with Dr. Rowland Hill's " central stream " as there would be no specified term of office in such an intermediate grade. It would cost money. But no just solution can avoid that.

Stratford-on-Avon. E. O. EVANS.

SIR,—The last sentence of Dr. Rowland Hill's letter (Sept. 7) surprises me in more ways than one, but chiefly because there was never any intention when the career grade was originally discussed by Professor Strachan's committee (of which I was a member) that it should be confined to certain narrow and routine hospital work outside the main clinical streams. If my memory serves me correctly the grade was suggested to meet the needs of hospitals, in particular those where there were no senior registrars. It was also felt that this might prove a solution to the registrar problem, and the point made by Another Senior Registrar in the second paragraph of his letter (Sept. 7) was advanced at that time. The recommendation went forward to the Central Consultants and Specialists Committee and was then referred to the regional consultants and specialists committees for their views. Unfortunately the old bogy of the supposed machinations of the Ministry, and the fear that a cheap consultant grade might be exploited by them was too strong ; so that it was the consultant members of the profession itself who turned their face against the idea—*before consultation with the Ministry on the matter.*

Queen Elizabeth Hospital, Birmingham, 15. B. N. BROOKE.

A NEW DISEASE ?

SIR,—Dr. Sinclair (Sept. 14) has given us a masterly demonstration of how to correct a difficult Latin text and many of us will be grateful for his clear translation. For most of us, however, Dr. Sinclair's scholarly approach is unattainable. Even though we now have his translation to augment our researches in *Lewis and Short* we may still be puzzled by some of the Latin words. Our sons do not possess the relevant crib so we must turn to the first edition of Fracastoro's poem and plod through it letter by letter.

Dr. F. N. L. Poynter has kindly shown me the first edition (1530) in the possession of the Wellcome Historical Medical Library. As expected, Dr. Sinclair's predictions are true. In addition I note that it is *cognomina* not *cognomine*, and that there are commas after *Syphilus* and after *noctes* ; the poem is also peppered with various accents.

I am still worried by the first word of the last line quoted by Dr. Irvine. Dr. Sinclair says it cannot be *Syphilidenque*. In the first edition (where *que* is usually abbreviated to *q* ;)

1. Rivlin, S. *Practitioner*, 1956, **176**, 541.

the word is given as *Syphilidèn q* ; . I should have thought that *Syphilidenque* was acceptable modern printing. The spelling *Syphilidemque* (i.e., *m* instead of *n*) is not found until a later edition of the poem. Perhaps Dr. Sinclair can enlighten me on this point ?

Guy's Hospital, London, S.E.1. C. G. A. THOMAS.

INADEQUACY OF GENERAL ANÆSTHESIA FOR ABDOMINAL OPERATIONS

SIR,—Dr. Loder's article of Sept. 7 encourages me to record some observations which I have been meaning to publish for many months.

I believe him to be perfectly correct in assessing the shock responses shown by patients to major surgery as due to autonomic stimulation. He goes on to describe what seems to me a complicated method of blocking the autonomics, in order to produce a comparatively shock-free patient at the end of operation. His method includes the injection of local analgesic agents by both the anæsthetist and the surgeon, along with general anæsthesia and routine blood-transfusion.

Since developing the technique of "controlled hypotension and postural ischæmia to reduce bleeding in surgery," [1] both Dr. Enderby and I have been struck repeatedly by the remarkably good condition of even the very frail and ill patients subjected to autonomic blockade. Because of this I studied the effects in a series of over 300 major gynæcological cases.

A large number of these operations were the more blood-letting ones, such as vaginal hysterectomy with anterior and posterior colpoperineorrhaphy, and Fothergill's operation. About a third were abdominal hysterectomies and Wertheim's operations. I extended the field of investigation deliberately to almost every type of major surgery. I found that by using an intravenous autonomic blockade I could produce extremely light anæsthesia with thiopentone and relaxant induction followed by gas-oxygen-pethidine maintenance, and the patients were screened against response to surgical shock. They remained pink, with a dry skin and no significant tachycardia. They recovered consciousness quite quickly, and showed no mental exhaustion, which Dr. Loder describes. Above all, when correctly postured, there was minimal bleeding at operation, and blood-transfusion was seldom necessary.

I have had many more opportunities to study these effects since coming to Bristol, where the technique has been used in thoracic, plastic, and neurological surgery, as well as for abdominoperineal and other major abdominal operations. Blood-transfusion is only used to replace such little blood as might be lost. I should like to encourage Dr. Loder to acquire the art of intravenous autonomic blockade, through a simple little Gordh needle, which would save him hours of patient work, and save the blood-bank bottles and bottles of blood. In the same issue of *The Lancet* as Dr. Loder's article is an appraisal of halothane. This interesting new inhalation anæsthetic also provides some degree of autonomic blockade.

In discussion with Dr. M. Johnstone, I discovered that he too felt that the well-being of the patients was due to the measure of autonomic blockade provided by the drug. Since this discussion I have been using halothane. It seems that, as with the intravenous technique, the response of the individual patient varies according to what I like to call the patient's "autonomic tone." It seems, therefore, that those patients with a high autonomic tone, in whom one would have had to use a large intravenous dose to produce a satisfactory autonomic blockade, would need to be taken very deep with halothane anæsthesia alone.

Such a course, in my opinion, is undesirable. I have been using very small doses of intravenous blockers to act, as it were, as a basal dose. Subsequently it has been necessary to use only quite light halothane anæsthesia, added in order to bring the patient down to the correct level of hypotension for good operating conditions and good postoperative results. I feel very strongly, from this experience and the gratifying results achieved that patients undergoing major surgery should no longer be denied the protection which autonomic blockade provides.

This argument becomes very hard to sustain in the face of the views of such an undoubted authority as Dr. Cecil Gray in his "Reflections on circulatory control" (*Lancet*, Feb. 23, 1957). He would have us use hypothermia in every case of induced hypotension. Such a procedure would render all but a few cases impracticable, and completely neglects the tremendous advantages which the technique has brought not only to plastic surgery but indeed, as I have tried to show, to most cases involving major surgery of any kind.

1. Enderby, G. E. H., Pelmore, J. F. *Lancet*, 1951, i, 663.

Bristol, 4. JOHN F. PELMORE.

SIR,—"Gad Sir, the feller can't give an anæsthetic!" Dr. Loder must be prepared to encounter this time-honoured type of reaction from many attempting to throw out a squid-like cloud over their determination not to undertake the relatively laborious procedure that he describes.

For my part, I applaud his efforts to give his patients the maximum possible degree of protection—which should rightly be our aim and object. Whilst I do not necessarily use the techniques that he describes, I strongly support his contention that nerve-blocking together with general anæsthesia best fulfils this criterion in most cases of major abdominal surgery.

London, S.W.15. G. C. STEEL.

WATER-RATES IN LONDON SURGERIES

SIR,—Many London practitioners must have felt aggrieved, as we did, when the recent re-valuation sent our water-rates soaring. After some correspondence with the Metropolitan Water Board we have stumbled on a closely guarded secret—that a 40% reduction of water rate is allowable on surgery premises occupied only by a caretaker. This is according to the Metropolitan Water Board Act of 1927, so we have been paying 66% excess water-rate on two surgeries for twenty years. It is a pity that there is no way of recovering this overpayment from the Metropolitan Water Board.

Many general practitioners who live away from their surgeries may be interested in our discovery.

W. BELTON
London, E.17. M. BELTON.

A FATAL CASE OF CHICKENPOX

SIR,—The harmless varicella seems to be changed into a serious disease with severe skin lesions and an atypical rash after exhibition of the adrenocortical steroids. Not long ago I was asked to see a case that was causing anxiety and had been diagnosed as "rickettsialpox" by a puzzled clinician. The danger of confusion with smallpox was very much appreciated. The patient, a young woman, looked like a case of chickenpox with one extensive area of skin sepsis, but she was running a very high temperature and was obviously very ill. She was being treated with cortisone. About this time a very illuminating editorial appeared,[1] and I advised that the cortisone be stopped at once. This was done and she made a good recovery.

One cannot help associating these iatrogenic deteriorations in a hitherto harmless disorder with another valuable editorial [2]—on pancreatitis and cortisone. Baar and Wolff [3] described pancreatic necrosis in cortisone-treated children and Marczynska-Robowska [4] and Pender [5] wrote on the same subject.

The legitimate treatment of allergic manifestations of immunological distortions with the adrenocortical steroids

1. *Brit. med. J.* 1957, i, 511.
2. *Lancet*, 1957, i, 828.
3. Baar, H. S., Wolff, O. H. *Ibid*, p. 812.
4. Marczynska-Robowska, M. *Ibid*, p. 815.
5. Pender, B. W. T. *Ibid*, p. 409.

(i.e., in conditions such as asthma, diffuse lupus erythematosus, periarteritis nodosa, and similar conditions, where most other forms of treatment fail or are disappointing and the outcome may be serious) should not, it is reasonable to suggest, be confused with the use of these substances in mild disorders with the object merely of improving symptoms or dispelling a rather disfiguring rash.

The apophthegm of Francis Bacon seems singularly inappropriate here: "He that will not apply new remedies must expect new evils; for time is the greatest innovator."

Epping, Essex. FRANK MARSH.

THE WOLFENDEN REPORT

SIR,—The letter from Dr. Learoyd (Sept. 14) may well prove to be the opening round of an extensive correspondence on the Wolfenden report. May we take this opportunity of appealing to those members of the profession who intend to enter the debate to make it clear in what capacity they express their views? In this respect Dr. Learoyd is honest. He states that he is a general practitioner; is it in this capacity that he makes the rather wild generalisation that psychiatrists are unfit to deal with practical affairs? If Dr. Learoyd has extensive knowledge of psychiatrists in general and those in particular who gave evidence to the committee, let him say so. If he has extensive knowledge of homosexuality, again let him say so. If, on the other hand, his views are the expression of outraged emotions let us know that too, so that we may judge just how valid his opinions are likely to be. Such phrases as "the coal face of psychiatry" (whatever that may mean) ill become the columns of a scientific journal.

It is not the purpose of this letter to point out all the fallacies in Dr. Learoyd's communication. He states that "the committee seems to have the haziest idea of the natural history of homosexuality"; it is clear from what Dr. Learoyd goes on to write that he has even less. On what grounds, for instance, does he state that there is little animosity against necrophilia and bestiality because these practices are not likely to appeal to many, and that the habit of homosexuality is likely to spread? Are these views based on personal work on the subject of homosexuality?

We are psychiatrists engaged in the treatment of convicted homosexuals. Whilst we do not pretend that (despite our training) we are completely free of prejudice or unconscious bias in relation to this emotionally charged topic, we can at least honestly say that we have some experience of the subject. May we express the hope that others who intend to state their views will consider soberly on what experience their opinions are based?

London, W.1. LEOPOLD H. FIELD
R. CEDRIC SIMPSON.

RENAL FAILURE FOLLOWING AORTOGRAPHY

SIR,—Dr. Gregg, in his letter of July 27, mentions some interesting aspects of renal aortography. Whilst not denying that the contrast obtained by accurate placement of the catheter tip in the renal artery is superior to that obtained by other methods, this method suffers from its failure to demonstrate aberrant renal vessels and as a primary arterial investigation it is inadvisable.

In the investigation of the renal aspects of hypertension, no angiogram can be regarded as complete until the whole pattern of both renal vessels is demonstrated.

With further reference to the placement of the catheter tip, it has been our practice to place the catheter above the origin of the renal vessels, since we have found that by placing the catheter below, retrograde filling occasionally fails to occur in patients with a rapid circulation.

Furthermore, we are not entirely convinced that a small quantity of contrast medium introduced directly into the renal artery is likely to have a lesser chemotoxic effect on the kidney than an injection of a higher percentage strength of contrast medium into the aorta.

We have, as Dr. Gregg suggests, on occasions filled smaller branches of the aorta but with no ill effects, and in view of Gayliss and Laws's work,[1] we are inclined to believe that aortic dissection is probably responsible for many of the complications so frequently labelled "chemotoxic."

Johannesburg. ERIC SAMUEL
MICHAEL DENNY.

VARIATIONS ON A NEUROSOPHICAL THEME

SIR,—In your leading article of Sept. 7 you comment upon Dr. Gooddy's comparison between the circulation of the nerve impulse and the circulation of the blood. Whatever the scientific evidence in favour of his thesis, you clearly regard it with abhorrence because it smacks of physical determinism, which, in your own words, "is an implicit rejection of the notion of free-will."

I venture to think that the reason for your aversion from determinism is not justified by logical analysis. Perhaps your aversion is aggravated by the use, when referring to the course of a nerve impulse, of the word *circle* which suggests the rigid repetition of the geometrical figure. Dr. Gooddy doubtless used this word to facilitate comparison with Harvey's concept of the movement of the blood, but if we substitute *circuit* we retain the property of regular succession and necessary connection implied by *circle* without accepting its unvarying repetition. This substitution does not affect Dr. Gooddy's meaning as far as my argument goes, because the properties of endlessness and dependence are still present, but it is easier to envisage the complex interconnection of ten thousand million nerve-cells as a *circuit* instead of a *circle* or even a *circulation*.

Now in Dr. Gooddy's view the neuronal circuit would be "closed" (to use the terminology of the physicists) because no external control is incorporated. Each event is succeeded by another event in infinite sequence. At this point you raise your hands in horror and say "But this is determinism—how can a man be responsible for his actions if each action is the result of an infinite chain of inevitable events?" Determinism it is, Sir, but his actions are entirely his own.

The only exclusive alternative (and, therefore, the one which you would favour) to Dr. Gooddy's hypothesis is a nervous system in which the circuit is not endless and dependent, because some external factor is able to control the sequential passage of the nerve impulse. By external factor I do not mean the external world of which we are aware through our sensory nerve-endings because (to take an extreme example) to torture a person until he confesses to a crime he did not commit negates his free-will however his nervous system functions. I refer to an extrasensory factor of which we are unaware and which can only operate if the circuit is discontinuous. Whether this factor is chance (the random selection of nerve impulses from a store, for instance) or an omnipotent, omnipresent deity does not affect the conclusion that because of it a person's actions are not wholly his own, and his responsibility for them is correspondingly decreased. The influence of blind chance upon cerebral processes is also exemplified by an epileptic discharge, and it is precisely under such circumstances as epileptic automatism that a patient is held not to be responsible for his actions.

No, Sir, it seems to me that determinism is not only compatible with free-will, but is necessary for it. Freedom of choice is an everyday experience, and, even though the choice is an event in the passage of a nerve impulse through an endless circuit, it is none the less our own. In

1. Gayliss, H., Laws, J. W. *Brit. med. J.* 1956, ii, 1141.

theory our choice might be predictable by a super-intellect which could determine the pathways of our nerve impulses and interpret their significance without affecting their course, or (to express the same thing in another way) which could predict our decision by discovering all the factors, conscious and unconscious, which had influenced us, without our being aware of the investigation. Such an event we believe to be impossible, but if we suppose that it could be achieved it is clear that such theoretical predictability does not reduce our moral responsibility in making a decision any more than my feeling, from my knowledge of him, that a man is going to cheat at cards excuses him when, in fact, he does cheat.

In conclusion it may be stated that if the activity of the brain is composed of nerve impulses in endless and dependent circuit, then the mind that is that brain is able to reach its decision by a process of logical thought in which, because it is not subject to external control, we recognise free-will. The philosophical implications of determinism are not to be feared.

London, W.5. J. HOWELL EVANS.

TRANSMISSION OF YAWS

SIR,—I am afraid that Dr. Cicely Williams's answer (Sept. 7) to my question about the geographical range of yaws does not really answer it. Most of the conditions which, she says, encourage the spread of yaws occur (or have occurred within living memory) in co. Kerry and Tierra del Fuego. I wonder if *Treponema pertenue* is near enough to a free-living parasite to demand a minimum atmospheric temperature for successful transmission. Treatment is so damnably efficient that we shall probably never know.

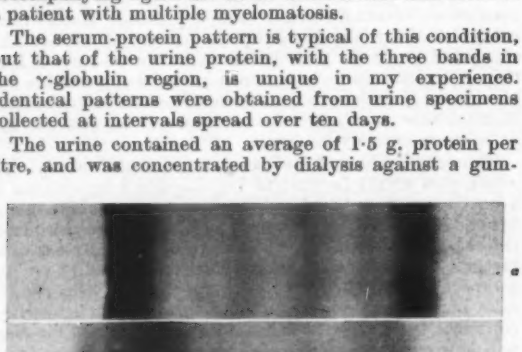
"HARRY HAWKE."

UNUSUAL URINE PROTEIN IN MYELOMATOSIS

SIR,—The two electrophoretic patterns shown in the accompanying figure are those of the serum and urine of a patient with multiple myelomatosis.

The serum-protein pattern is typical of this condition, but that of the urine protein, with the three bands in the γ-globulin region, is unique in my experience. Identical patterns were obtained from urine specimens collected at intervals spread over ten days.

The urine contained an average of 1·5 g. protein per litre, and was concentrated by dialysis against a gum-acacia solution. Electrophoresis was carried out in a barbitone buffer, pH 8·6, at 100 volts for 15 hours.



The electrophoretic patterns of serum (*a*) and urine (*b*) proteins in a case of multiple myeloma.

In the examination of some 40 cases of myelomatosis I have never encountered a Bence Jones protein which gave other than a single band upon electrophoresis under the above conditions, neither have I seen any report of more than one band being obtained, except at an acid pH.

I shall be interested to hear of any similar results which may have been obtained in other laboratories.

Llandough Hospital, Penarth, Glam. A. J. CUMMINGS.

MATRIARCHY

SIR,—Your correspondent has made some penetrating observations on the nurse-patient relationship in his Personal Paper (Aug. 24). What would he have concluded had his ward been staffed in part by male nurses? It is notorious that these individuals tend to display amusement, if not impatience, at the "aura of authority" generated by certain of their female colleagues. It is equally notorious that these same men are often efficient nurses, with a talent for gaining hospital prizes and the respect of their patients.

Perhaps this helps to explain the resentment many women feel on encountering this male invasion of "their" profession. (What happened when women invaded Medicine?) They have tried to "make a corner," and establish matriarchal authority over both sexes as the essence of nursing; but the tide is bound to run against them as the individual nurse becomes increasingly a "specialist in inter-personal relationships." (Observe the recent emphasis on psychology for general nurses.)

Your correspondent has aptly stated the paradox of a job that seems to attract by virtue of its disadvantages. He might care to be reminded that this attraction can persist, for women as well as men, even where the "matriarchal subsociety" is cracking.

I must confess to prejudice in this matter, and sign myself

MALE S.R.N.

THE LIVER IN HÆMOCHROMATOSIS

SIR,—In their letter of July 20, Professor Gillman and his associates state that "the findings of Higginson et al. in their 1957 studies *seem* to contradict those of their 1953 report and, moreover, are apparently not in conformity with the reports of other workers in the Union, all of whom seem to agree that portal cirrhosis associated with severe siderosis is the most common variety of cirrhosis encountered among Africans in the Union."

As one of the other workers whose name has been quoted in this letter, I should like to reply briefly to some of the points mentioned in his letter:

(1) The concept of what constitutes a cirrhosis of liver in contradistinction to hepatic fibrosis has undergone a radical change since Strachan,[1] Becker,[2] Gillman and Gillman,[3–5] or Higginson [6] published their surveys. I classified cases as "early" cirrhosis in 1944, which I would now regard as simple portal fibrosis. The criteria for a true cirrhosis have been clarified and so to a certain extent have the possible pathogenetic pathways. At any rate, in my necropsy liver material from both Europeans and Africans on the Witwatersrand (and basing one's classification on the morphological criteria proposed by Himsworth [7] and Goldblatt [8]) *the commonest variety of cirrhosis encountered amongst both Europeans and Africans in this part of South Africa is post-necrotic cirrhosis.* This type of cirrhosis is quite unrelated to the presence or degree of siderosis.

(2) I have recently had the privilege of a visit from Prof. Paul Steiner, who independently reviewed my material. With his permission, I quote from his report on the African cases: "The post-necrotic type comprised about two-fifths of all cases The Laennec type, which is probably related to the post-necrotic type, accounted for another two-fifths. A small proportion were classified as pigmentary. Many other cases had appreciable amounts of pigment but it did not appear to be related to the fibrous tissue. Most of the cases classified as pigmentary were of the monolobular type, and if the pig-

1. Strachan, A. S. M.D. thesis, Glasgow, 1929.
2. Becker, B. J. P. *Leech*, 1944, **15**, 15.
3. Gillman, J., Gillman, T. *Arch. Path.* 1945, **40**, 239.
4. Gillman, J., Gillman, T. *Lancet*, 1948, i, 169.
5. Gillman, J., Gillman, T. Perspectives in Human Malnutrition, New York, 1951.
6. Higginson, J., Gerritsen, T., Walker, A. R. P. *Amer. J. Path.* 1953, **29**, 779.
7. Himsworth, H. P. Lectures on the Liver and Its Diseases. Oxford, 1947.
8. Goldblatt, H. Transactions of the 6th Conference on Liver Injury. Josiah Macy, jun., Foundation. New York, 1947; p. 9.

ment could be removed from them they would be classified as Laennec A or B, or post-necrotic."

(3) There is no doubt about the frequency of hepatic siderosis in Africans in most parts of the Union. It does tend to disappear in the Southern Cape [9] and in Portuguese East Africa, although all arguments in relation to inadequate diet apply equally forcefully in those regions, and moreover the incidence of cirrhosis in Africans and Coloureds in the Southern Cape and in Portuguese East Africa as high as elsewhere in the Union. Incidentally our students here have for long been taught how to distinguish between African visceral siderosis and hæmochromatosis.

(4) I doubt whether many in this country would agree with the view of Gillman and his associates that acute infectious or "epidemic" hepatitis is uncommonly seen clinically amongst Union Africans, though of course proof of the viral nature of these clinical cases and confirmation of the viral ætiology of post-necrotic cirrhosis of the liver in Union Africans await the introduction of a satisfactory objective test for present or past virus hepatitis. It is possible that malnutrition may predispose the liver if damaged by other factors towards the development of cirrhosis, though no clear proof of this exists.

University of the Witwatersrand, Johannesburg. B. J. P. BECKER.

INTRAVENOUS ADMINISTRATION OF METHYL PHENIDATE

SIR,—Methyl phenidate (methyl-1 phenyl-2 piperidyl acetate, 'Ritalin') has been administered intravenously after an anæsthetic to 100 outpatients with the primary object of speeding recovery and removing all trace of hangover.

The dosage was about 20 mg. per 10 stone body-weight. The anæsthetics used were thiopentone, nitrous oxide and oxygen, trichlorethylene, and pethidine; and the duration of operation was generally less than an hour.

Though the awakening-time was not notably advanced, when consciousness was fully regained patients appeared full of zest and bright, and had a very good appetite. There were 2 exceptions.

No antagonism was found to alcohol, nor to the clouding following chlorpromazine; but the effect of methyl phenidate on muscle-tone when chlorpromazine was used proved interesting.

A year ago a combination of chlorpromazine and pethidine was used in conjunction with a thiopentone/nitrous-oxide/oxygen system to afford a smooth anæsthetic in the elderly over periods up to three hours. When the patient had been returned to the ward, he presented one of two pictures: either he was sufficiently recovered to object to the presence of an airway, but completely oblivious to the dangers of his own obstructing tongue; or there was noisy breathing (probably due to spasm of pharyngeal muscles) with obviously enlarged veins and an off-pink colour. Administration of methyl phenidate rectified this undesirable aspect of the recovery in about three minutes. It was also found to speed the return of normal muscle-tone in powerfully built patients who showed muscle fibrillation, stertor, and cyanosis following the use of thiopentone, nitrous oxide and oxygen, and trichlorethylene.

A notable side-effect was wakefulness without loss of analgesia.

An elderly woman, after an extensive operation on the humerus, remained awake the entire night, but was comfortable and content, and slept well the following night. This effect lasted sixteen hours in one case, and then sedatives were granted. But when the wakefulness was limited to an hour or two, there was the satisfaction of knowing that the patient could look after himself in the event of vomiting and was ventilating adequately.

Sympathetic stimulation was not observed. The hypotension that often follows the administration of chlorpromazine was not affected. It would appear that the outstanding feature of the intravenous use of methyl phenidate in anæsthetic practice is that it is a powerful barbiturate antagonist.

I am indebted to the writings of J. Van de Walle (Paris) concerning the use of intravenous methyl phenidate, and should like to thank Ciba Laboratories Ltd. for providing 'Ritalin' in a form suitable for intravenous administration.

Birmingham Accident Hospital. REGINALD GRAHAM.

MEDICINE AND THE HUMANITIES

SIR,—In his paper on Medical History (Aug. 31) Dr. Agnew tells us that the University of Adelaide has created a readership in humanities for medical students. This is a bold and necessary step and let us hope that the example of Adelaide will be followed by other universities.

In fact humanistic culture is as important as natural scientific culture for the practice of medicine. As physicians we have to act upon men and as man is body, mind, and spirit, we cannot limit ourselves to the study of the basic medical natural sciences, physiology, pathology, nosography, but we must also know the human mind in its various manifestations embodied in the term "culture," a knowledge developed in psychology, sociology, and history. More than that, we must take into consideration the human spirit, that mysterious power that makes us aware of our uniqueness, our liberty, our creativity, and directs us towards transcendent values. Such knowledge, if we can use that term, is embodied in the lofty thoughts of the great philosophers and religious leaders. Psychology, sociology, history, and philosophy constitute the humanities, that is the sciences referring to the real human characteristics, the human mind and the spirit, whereas the physical sciences, physiology, pathology, and nosography, deal with the aspect of man common with other natural beings. History of medicine is the great link between the physical medical sciences and the humanities.

Some time ago that great medical educator, Alan Gregg,[1] was writing "How meagre the cultural baggage, how callow the manners, how unexercised the imagination and the sympathies of our medical students must remain if we do not open for them the resources of Humanism for the enrichment of their training. How can we expect such a one to have the spiritual values that will enable him to combine effectively with patients in the bewilderment, loneliness and anxiety of illness."

London, W.1. A. P. CAWADIAS.

SEX IN ANENCEPHALUS

SIR,—In anencephalus there is a striking excess of affected females. Various explanations have been suggested for this finding, such as selective affection of females, disproportionate embryonic or early fœtal mortality of affected males, &c. However, in view of recent findings on aberrations of sexual differentiation in man the possibility should be explored that an error of sexual differentiation may underly the apparently disturbed sex-ratio in this condition. During the last twenty months one of us (A. E. C.) has studied the external and internal sexual differentiation of 12 anencephalic babies (4 males, 8 females) born at Queen Charlotte's Hospital, London, and determined the status of the nuclear sex chromatin. In each case the "nuclear sex" agreed with the post-mortem findings of the anatomical sex. As, however, the anencephalic defect is variable, and only some of the defects may be associated with anomalous sexual differentiation, we feel that study of further material will be necessary to confirm the findings of our limited sample. In view of the relative rarity of anencephaly we would be grateful for the help of colleagues who see such cases. We would suggest the following investigation:

(1) Nuclear sex determination on skin or "sexable" internal organs.

9. Thomson, J. G. Personal communication.

1. Gregg, A. *Bull. N. Y. Acad. Med.* February, 1941.

(2) Appearance of external genitalia, possibly with photograph.
(3) Appearance of internal genitalia and genital ducts.
(4) Histological appearance of both gonads.
(5) Appearance and size of the adrenal glands.
(6) Gestation age.

We would be grateful if interested workers could communicate to us their findings, or alternatively submit either histological sections or necropsy material. In the latter event we would like to suggest that a fragment of skin and both gonads be put into Bouin's fixative, and despatched to us as soon as possible after collection, together with information concerning points 2, 3, 5, and 6 listed above.

Keats' House, Guy's Hospital, London, S.E.1. PAUL E. POLANI.

The Bernhard Baron Memorial Research Laboratories, Queen Charlotte's Maternity Hospital, London, W.6. A. E. CLAIREAUX.

MECHANICAL FACTORS IN ATHEROSCLEROSIS

SIR,—Dr. Robertson and I are grateful to Dr. Hamilton (Aug. 17) for drawing our attention to the proper priority which should have been given to Dr. J. C. Paterson's name in reference to intimal hæmorrhage in our report.[1] I must confess that in drawing up our list of references I had Dr. Paterson's later paper before me and carelessly overlooked his earlier one on the same subject.

Department of Pathology, Royal Victoria Infirmary, Newcastle upon Tyne, 1. J. B. DUGUID.

STREPTOCOCCAL INFECTIONS AND PREGNANCY

SIR,—There is a good deal of evidence on general grounds to incriminate the streptococcus as an infecting agent which might have important effects in early pregnancy, and recently it has been accused of possibly accounting for unexplained fœtal abnormalities.[2]

This hypothesis is quite rational, and though no significant association at the clinical level has been demonstrated there is some circumstantial evidence in its favour on the statistical side. When the regional variations of mortality from congenital malformations in the first year of life are compared with the variations of mortality from streptococcal or post-streptococcal diseases, a high level of correlation is obtained. It is of the order $+ 0{\cdot}7$, $t = 3{\cdot}15$. The rates for the decennium 1932–41 are shown in the accompanying table.

Region	Congenital malformations (under 1 year, per 1000 live births)	Deaths per million living (aged 5–14 years)	
		Heart-disease	Nephritis
Greater London	5·29	60·5	27·6
Remainder of South-east	5·37	44·6	22·4
North I	6·23	85·4	39·8
North II	6·46	66·8	29·1
North III	6·15	78·3	33·3
North IV	6·96	86·6	36·1
Midland I	6·38	78·4	33·5
Midland II	6·25	60·7	31·4
East	5·95	41·9	21·6
South-west	6·27	49·7	28·6
Wales I	6·92	105·0	42·7
Wales II	6·26	64·9	28·7

In view of the possibility that the streptococcus is implicated in this and in other disturbances associated with pregnancy,[3] it seems justifiable to arrange controlled field trials to test the influence of prophylaxis against streptococcal infection in the early months of pregnancy, on the same lines as prophylaxis against recurrences of rheumatic fever. The new long-acting preparations of penicillin and sulphonamide would be useful here. It would be of great interest to know whether they had a beneficial effect on the incidence of fœtal abnormalities and of the complications of pregnancy and labour—particularly toxæmia, which remains the chief hazard to the life of the expectant mother.

Glasgow, W.4. T. W. BUCHAN.

1. Duguid, J. B., Robertson, W. B. *Lancet*, 1957, i, 1205.
2. Pleydell, M. J. *Ibid*, p. 1314.
3. Buchan, T. W. *Brit. med. J.* 1951, ii, 1011.

RECURRENT APHTHOUS STOMATITIS

SIR,—Your annotation of Aug. 10 prompts me to offer some comment based on observations made in the treatment of this disease.

In a paper to be published [1] my colleagues and I call attention to the prevalence of herpetiform lesions and their treatment with gamma-globulin. It is our belief that aphthous ulcers are not caused by herpes virus but by an unknown virus since patients suffering from these ulcers have a low antibody titre against herpes virus while those suffering from herpetic stomatitis frequently have a high antibody titre against the homologous antigen.

Since various forms of stress (traumatic, physiological, or emotional) seem to precipitate a crop of aphthous ulcers, we postulated that the resulting increase in endogenous hydrocortisone might interfere with the immune mechanism. Since gamma-globulin contains antibodies against various viruses, we believed that this blood fraction would contain antibodies against this unknown virus.

We have treated approximately 50 patients who received varying doses from 3 to 10 ml. Some patients required one injection, while others received additional injections for several days or several weeks. In most instances, prompt recovery was observed. One of these patients suffered from a severe case of Behçet's syndrome and the response was dramatic after many other forms of therapy failed, including chlortetracycline.

Others may wish to try this treatment for a troublesome condition which plagues the patient and humbles the physician and dentist.

Merck Sharp & Dohme Research Laboratories, West Point, Pennsylvania, U.S.A. LYON P. STREAN.

ACNE VULGARIS

SIR,—In January you very kindly published [2] a lecture of mine on this subject. There are two items of information which I should now like to add.

(1) At the time the lecture was delivered I was not aware of the interesting paper by Van Scott and MacCardle [3] published in the United States, in which they stated that the earliest change in acne is hyperkeratinisation of the excretory duct of the sebaceous gland which results in the deposition of a keratinous plug in the follicular neck. They tentatively suggested that the products of the sebaceous gland may "biochemically initiate the hyperkeratosis that leads to the principal morphological lesion of acne." If confirmed their observation is of considerable importance, and their suggestion might well be considered in relation to the work of Dubovyi [4] concerning the increase of 17-ketosteroid excretion through the sebum in acne vulgaris.

(2) During the past ten months I have treated more than 35 cases of acne vulgaris both in males and females with tablets each containing 50 i.u. serum-gonadotrophin. The standard dose has been 2 tablets per day but sometimes twice this amount has been given. An important matter in this treatment is that the tablets must be dissolved in the mouth. At first I regarded this therapy, though it was originated by Aron-Brunetière [5] with considerable scepticism, and it will require quite a long period of observation to determine whether my first

1. Strean, L. P., Williams, B. H., Prichard, J. *Oral Surg.* (in the press).
2. MacKenna, R. M. B. *Lancet*, 1957, i, 169.
3. Van Scott, E. J., MacCardle, R. C. *J. invest. Derm.* 1956, 27, 405.
4. Dubovyi, I. *Vestn. Vener. Derm.* 1955, 2, 22.
5. Aron-Brunetière, R. *Sem. Hôp. Paris*, 1954, 24, 1513; *Ibid*, 1956, 32, 2094.

impressions were merely fortuitous. It will also require considerable investigation to determine whether—if these impressions are confirmed—the corollary that acne vulgaris is a manifestation of "incomplete pituitary insufficiency" can be considered. At the present time I wish merely to record that of these cases (many of them proved to be resistant to other types of treatment) 60% showed great improvement, 25% improvement, and 15% failed to respond.

London, W.1. R. M. B. MACKENNA.

HYPERTONIA OR UNEVENTFUL HIGH BLOOD-PRESSURE

SIR,—The paper by Dr. William Evans and your leading article (July 13) point up our present lack of insight into the mechanisms of high blood-pressure and the course of hypertensive disease. Dr. Evans's syndrome of "hypertonia or uneventful high blood-pressure" seems to include two different situations associated with transient elevations of blood-pressure. The case of the recruits we recognise as a common manifestation of vasomotor instability in youth which, particularly in those with familial predisposition, may develop into hypertension. The older group, with a comparatively benign course and labile, largely systolic rise in pressure, corresponds to what we term "arteriosclerotic hypertension"; in this, arterial pressure varies with cardiac output and falls with rest, reassurance, incantation, or sedation. But Dr. Evans has no substantial evidence to show that the one group ages into the other.

Further, as your leader indicates, the crux of the problem is the *average* level of arterial pressure over months and years, rather than the pressure during a single examination. We all know old people whose pressure is over 200 mm. Hg systolic every time it is taken; no-one knows what it is in the intervals, and these are usually fairly long. Dr. Evans's concept seems also to include some patients with persistent diastolic hypertension who are fortunately endowed with a rich and durable "vital rubber." His article brings to mind Osler's address on High Blood Pressure, Its Associations, Advantages and Disadvantages.[1] But Osler's dialectic skill was hard put to demonstrate any remarkable advantages of this condition; the courses of Dr. Evans's 50 "hypertonic" oldsters were complicated in 1 by "encephalopathy" and in 12 by cardiac pain, and were terminated in 9 by myocardial infarcts. This record seems uneventful only by understatement. It is good to be reassuring, but only when one can do so on secure grounds.

We would not insist on acceptance of any one of the systems of classification of the "primary" hypertensions,[2–4] since none is definitive and all are more or less subjective. Still, conformity to some one of them facilitates communication. Dr. Evans seemed to have formulated his concept by disregarding these and introducing an hypothesis based on no more, and perhaps less, objective evidence than anyone else has. In particular, none of these systems defines "malignant hypertension" as a separate entity; each indicates that it is probably a syndrome of "accelerated" and severe hypertension; each admits the possibility that some new ætiological factor has been added in the "malignant syndrome," but none hold this to be demonstrably true.

Your editorial notes the tendency of some secondary hypertensions to persist after removal of their causes. Bearing on this clinical observation are the experiments[5] in dogs with chronic renal hypertension; these were found to have shifted the "set" of their baroceptors upward so that a hypertension initially of renal humoral origin was ultimately maintained by vasomotor mechanisms. These experiments imply that hypertension from any cause may be self-perpetuating; they suggest that, with repeated and prolonged pressor reactions, it may be progressive. The latter seems to be the case in patients with apparent "hypertonia"—i.e., transient hypertension without clear-cut hypertensive vascular disease—in whom hypertension ultimately becomes sustained. Further, as you indicate, there is abundant evidence that sustained diastolic hypertension as such is damaging.

For these reasons, we are now more prone than heretofore to recommend anti-hypertensive treatment to patients with mild diastolic hypertension who show no signs of hypertensive vascular disease, the more so as the evidence indicates that these patients are prone to premature complications of atherosclerosis. We are influenced in this decision by the hope that some of them may, after prolonged intervals of normotension, "re-set" their baroceptors down; we believe anti-hypertensive treatment may prolong life and well-being. We have no doubt that some may regard this as unnecessary meddling with a "benign" process. We know that it will be hard for us to prove that we are doing more good than harm. But it will require more definitive criteria than are presently available to enable us to separate out, for reassurance and expectant treatment, patients with persistent diastolic hypertension whose medical histories will be truly uneventful.

Research Division,
Cleveland Clinic Foundation,
Cleveland, Ohio.

HARRIET P. DUSTAN
A. C. CORCORAN.

1. Osler, W. *Brit. med. J.* 1912, ii, 1173.
2. Page, I. H., Corcoran, A. C. Arterial Hypertension: Its Diagnosis and Treatment. Chicago, 1949.
3. Shroeder, H. A. Hypertensive Diseases: Causes and Control. Philadelphia, 1953.
4. Pickering, G. W. High Blood Pressure. New York, 1955.
5. McCubbin, J. W., Green, J. H., Page, I. H. *Circulation Res.* 1956, 4, 205.

TRACHEOTOMY TUBES AND CONNECTIONS

SIR,—Tracheotomies have always been performed to save life, and today there is a wider use for this operation. Failure in the management of these patients, however, can be the immediate cause of death.

In his article of Aug. 24 on tracheotomy tubes and connections, Dr. Bullough has raised several important points, and I should like to express some views based on experience at the Portsmouth Respiratory Unit.

All rubber perishes, and so special tubes may not be serviceable when wanted; it may take twenty-four hours or more to get a new one. This point is particularly important when only a few cases are treated each year.

The tube which we have used here for over two years[1] is a similar shape to the one shown by Dr. Bullough, but we make it from ordinary Magill's tubes found in any operating-theatre; the shape is formed by inserting a silver lining. We have stopped using the endobronchial cuff illustrated, since not only is a higher inflation pressure necessary (and this might cause tracheal ulceration) but also there is a greater tendency to air leakage with resultant inadequate ventilation.

We have never used a no. 12 tube; a no. 10 has always seemed adequate, and it would be interesting to know if the larger aperture required for the no. 12 tube has created other difficulties—e.g., delayed healing and increased scarring.

As regards the metal connection with suction piece, our experience differs from that of Dr. Bullough in several ways. Firstly, we consider a large suction catheter (whistle tip) to be of paramount importance and we prefer a no. 10 E.G. to the no. 6 E.G. used by Dr. Bullough. The larger size will clear the secretions more quickly and this may explain why we do not see "asphyxiation" in our patients. If a patient becomes blue during suction, this fact will probably be reported immediately; we consider any anoxic episode to be serious and to be avoided at all costs. Secondly, another important function of the suction catheter is to clean the tracheotomy tube. If a small catheter is used, the tube quickly furs up. Should a larger catheter then be used, a piece of encrusted secretions is likely to be loosed into the bronchial tree and this may well cause trouble. Thirdly, we find that metal tops to

1. Hodges, R. J. H., Morley, R. O'Driscoll, W. B., McDonald, I. *Lancet*, 1956, i, 26.

suction unions (Cobb) tend to stick, and removal can be difficult. We find Magill's suction unions with the rubber cap to be satisfactory.

As regards resistance in apparatus, we have tested standard equipment and the special equipment described by Dr. Bullough, using ventilation rates and volumes normally used with adult patients. The difference as shown on a recording spirometer was very slight, and we continue to use standard equipment. When an efficient flutter valve [2] is in use, the endotracheal pressure during expiration is usually zero and will not rise above $^1/_2$ cm. of water, and so the delay in emptying the lungs and the interference with venous return and cardiac output mentioned by Dr. Bullough will not occur.

The silver linings are made for us by the Endoscopic Instrument Company, 62, Shirland Road, London, W.9, and should be lubricated before insertion.

Portsmouth Poliomyelitis
Respiratory Unit,
Infectious Diseases
Hospital, Portsmouth. H. B. C. SANDIFORD.

A JOB ON THE BEACH

SIR,—May I as an ex-regular Naval officer who qualified in the "difficult thirties" be allowed to thank your peripatetic correspondent for his pat on the back on Aug. 10.

I do not suppose many of us expected to achieve any great professional distinction, one should start young to do that. Nevertheless the rewards have been sufficient; and if we possessed any particular merits, they can be attributed to a tradition and a training which was unique in its time.

There must be many Naval officers looking around for a job on the beach now. Those who have the ability and the guts to stay the course will not be disappointed in medicine as a life career in the real sense of the word.

"TOM BOWLINE."

OPTIMUM FLUORIDE CONTENT OF WATER

SIR,—It is encouraging to read in your issue of Sept. 14 (p. 537) that the World Health Organisation has expressed its approval of fluoridation of water-supplies, but unfortunately this declaration may not end all controversy on the subject. I believe that some of the confusion in the minds of laymen results from the different meanings given to the word fluoridation by those who are for or against it. For example, the W.H.O. report speaks of "natural fluoridation" in reference to the occasional occurrence of an optimum fluoride content in water before treatment, but the so-called anti-fluoridationists have never objected to water-supplies affected in this way.

May I suggest that W.H.O. and other interested bodies could clarify the issue by recommending primarily, not fluoridation itself, but rather an optimum fluoride content for water-supplies? No-one can object to an optimum as such, no-one does object to fluoride content as such, and I believe that no-one has suggested that the optimum content is far from the region of 1 to 2 parts per million. The opponents of (deliberate) fluoridation usually avoid discussion of what might constitute an optimum concentration, and their attitude is consistent only with the absurd theory that any concentration is wholesome so long as it has not been deliberately engineered by adding fluorides at the waterworks. There is, of course, some room for dispute about an optimum concentration, but this would be more profitable than the violent outcries against "mass medication" that seem to be provoked by use of the word "fluoridation." The general public and local authorities might readily accept the verdict of recognised expert bodies on the definition of optimum fluoride content, while wishing to reserve the right to decide for themselves whether or when to take any action necessary to achieve such a standard of wholesomeness in their water-supplies. Such action need not always be fluoridation at the works; sometimes more "naturally fluoridated" water could be brought into supply.

Other objections to unnecessary use of the word "fluoridation" are its similarity in sound to "chlorination" and the ugliness of such derivatives as anti-fluoridationist; use of the word might well be restricted to any necessary specific reference to the engineering operation of adding fluorides at the waterworks.

London, S.W.10. R. B. D. STOCKER.

2. Sandiford, H. B. C., McDonald, I. *Ibid*, p. 1014.

NUPASAL IN THE TREATMENT OF TUBERCULOSIS

SIR,—'Nupasal' (*o*-hydroxybenzal isonicotinyl hydrazone, or 'Salizid') is a derivative of isoniazid. It was found to have tuberculostatic activity in vitro at a concentration of 0·09 μg. per ml., which is about a third of the potency of isoniazid, weight for weight; in vivo, however, using the corneal test in mice, its activity is almost the same as that of isoniazid. It was shown to be five times less toxic than isoniazid and, consequently, much greater doses can be given—20–25 mg. per kg. body-weight. Its exact mode of activity still remains undecided, since no accurate method has been devised of distinguishing between isoniazid and nupasal in the blood. It is likely that it has some activity of its own, but it is also known that it metabolises partly to isoniazid, which will be responsible for part of the anti-tuberculous effect. Resistant organisms develop as readily as they do to isoniazid.

At first not much interest was taken in this drug, for it was felt that its activity was little superior to that of isoniazid, and its potentiality was not appreciated. Since 1954, however, when reference was first made to this substance,[1-3] clinical trials have been proceeding and all have been favourable, especially in freedom from toxic manifestations—particularly neurotoxicity, which is seen occasionally with isoniazid.

Katz [4] treated 39 patients with pulmonary tuberculosis for periods of four to sixteen months, giving doses of only 400 mg. daily, and considered the results as good as those with isoniazid. McCormack [5] treated 50 patients, using 1 g. daily together with streptomycin 1 g. twice weekly. The response, he thought, was excellent in 41 patients, and there was no evidence of neurotoxicity. In addition he gave nupasal to 13 patients in whom peripheral neuritis had developed during isoniazid therapy, and in all but 2 remission was complete. At the Richmond Veterans Administration Hospital in Virginia [6] clinical studies have been made, using doses up to 1·2 g. daily. No patient had the drug discontinued because of toxicity, and there were not even minor neurotoxic manifestations. At the same hospital this year [7] nupasal was given to 8 patients with tuberculosis who had had neurological or convulsive disorders; doses of 300 to 1200 mg. were used and the results were excellent. It was concluded that nupasal can be used safely and effectively as a substitute for isoniazid in the presence of neurological and convulsive disorders.

At Wrightington Hospital we have been using nupasal for the past two years in the inpatient treatment of genito-urinary tuberculosis, using a dosage of 25 mg. per kg. body-weight, and have been very satisfied with the results and absence of toxicity. Even in patients with a raised blood-N.P.N. (in whom the blood-levels of nupasal and isoniazid are much higher than normal), there has been a singular absence of untoward effects.

1. Nagley, M. M. *Lancet*, 1954, ii, 337.
2. Barry, V. C., Conalty, M. L. *Ibid*, p. 495.
3. See annotation, *Ibid*, p. 539.
4. Katz, S., McCormack, G., Storey, P. B., de Leon, A., Romansky, M. J., Marshall, E. E. jun. Transactions of the 13th Conference on the Chemotherapy of Tuberculosis, 1954, p. 374.
5. McCormack, G., Katz, S., Chambers, I., Gimble, A., Leonard, J., Schmidt, W., Shea, J. *Ibid*, 1955, p. 332.
6. *Quart. Prog. Rep. V.A.* 1956, **11**, 67.
7. *Ibid*, 1957, **12**, 58.

In addition we are now using this drug in a dose of 250 mg. four times daily as a routine with 'Therapas' and streptomycin in our three-month post-sanatorium domiciliary course of treatment. As yet we have seen no evidence of toxicity.

Much interest is now being shown in the use of isoniazid in larger doses than those used hitherto. Pyridoxine may reduce neurotoxicity, and clinical trials have been started using doses of up to 1 g. isoniazid with 250 mg. pyridoxine daily. As nupasal has been given in dosages of up to 3 g. a day, apparently without toxic effect, it may well prove possible to give such high-dosage isoniazid therapy in the form of nupasal without the co-administration of pyridoxine.

Wrightington Hospital, near Wigan, Lancs. J. G. GOW.

RELATIONSHIP BETWEEN NAUSEA AND/OR VOMITING IN EARLY PREGNANCY AND ABORTION

SIR,—With reference to Dr. Medalie's interesting paper (July 20), let me remark that while he clearly shows the actual inverse correlation between the occurrence of nausea and vomiting during the first three months of pregnancy on the one hand, and of miscarriage on the other, he does not proceed further to suggest the reason or reasons why things usually happen this way.

I believe that the hypothesis I advanced on this relationship as early as in 1933 [1] has been borne out by the facts. This hypothesis is that nausea and vomiting during the first three months of pregnancy develop on an allergic basis secondary to the histolysis which accompanies the fertilised egg's nidation into the submucous tissues of the uterus. A successful nidation leads to a considerable liberation of allergenic products of histolysis, but a poorly nidated egg, prone to miscarriage, liberates little or nothing.

This assumption has been corroborated by therapeutic results. I have treated—mostly with very good results—many severe cases of hyperemesis gravidarum by intramuscular injections of the husband's whole blood in increasing amounts (from 2 ml. to 20 ml.), after it has been shown that there are no blood-group and Rh-factor incompatibilities between husband and wife.

Clinica Corachan, Barcelona, Spain. P. PUIG Y ROIG.

ARSENIC AND TOBACCO

SIR,—Just six years ago, following the observations of Sir Ernest Kennaway on the presence of arsenic in tobacco, I gave you the figures in my own favourite brands.[2] The report of the Medical Research Council has prompted another look. For convenience, I repeat the results of 1951:

Brand	*Year*	*Lead* (*parts per million*)	*Arsenic* (*parts per million*)
My favourite pipe-tobacco	1951	96	32
	1957	4·8	2·5
A popular cigarette	1951	143	68
	1957	5·1	2·0
Havana Cigar	1951	414	170
Havana Cigar (presented last Christmas)	1956	260	128
Havana Cigar (a recent purchase) ..	1957	36	24

To those of us who feel that the major change in the growing and handling of tobacco in recent years has been in the use of arsenical sprays, and that the relation of this to lung cancer needs to be thoroughly investigated, the above results are at least encouraging, for the young will smoke while tobacco is available.

It is evident that tobacco can be produced without the use of arsenic sprays, or at least their residues can be avoided. It is to be hoped that public opinion will insist that tobacco joins iced lollies, dried liquorice extract, chicory, and pectin, in having a definite limit of contamination with arsenic.

London, S.E.1. J. H. OLIVER.

1. Puig y Roig, P. Síntesis Médica. Barcelona, 1941; vol. II, p. 277.
2. Oliver, J. H. *Lancet*, 1951, ii, 266.

Obituary

MICHAEL DOUGLAS STAUNTON
M.B. N.U.I., L.A.H.

Dr. Staunton, who died on Sept. 2 at his home at Swinford, co. Mayo, studied medicine at the Catholic University Medical School, Dublin, and at Mater Hospital, Dublin. After qualifying in 1911 he was appointed dispensary doctor in his native town of Swinford, and he held this appointment continuously up to the time of his death. He is survived by his widow and their six children, all of whom are doctors.

Dr. E. G. RECORDON

C. H. W. writes:

Esmond Recordon was well versed in the arts. Though only a very amateur pianist he was a keen listener and he did much to encourage and help young musicians whom he often entertained at his house. Drama also appealed to him and he was a regular supporter of the local repertory theatre. But it was as a connoisseur of painting that he really excelled. His taste, which was classical, turned more and more towards modern painting and he gradually acquired a valuable collection, including many of the impressionists.

I knew him well, and though we did not meet regularly we could pick up the threads just where we left off, however long the lapse of time.

Why was his friendship so valued? He had early acquired a philosophy which enabled him to come to terms with life. He could accept adversity. If he grumbled, he did so in such a way that somehow the outlook became less grim. He believed the best in men and often found the best. His sympathy and wisdom were there for the asking. Injustice infuriated him and he fought hard to defend its victim. These qualities combined with great shrewdness made him an admirable colleague. There was something about him slightly old-fashioned, almost naïve, which was endearing. Long before his final illness, while he was still comparatively young, thrombophlebitis greatly curtailed his activities, but he remained undaunted, adapting himself to the new way of life without bitterness. He cultivated serenity and it stood him in good stead. He enjoyed life, and he helped others to do so.

Appointments

BLOOM, H. J. G., M.D. Lond., M.R.C.P., D.M.R.T.: assistant in the department of radiotherapy, Middlesex Hospital, London.
BRISCOE-SMITH, J. H., M.B. Birm., D.P.H.: M.O.H., St. Marylebone, London.
CHRISTISON, JOAN R., M.B. Glasg.: assistant psychiatrist (S.H.M.O.), Craig Dunain Hospital, Inverness.
ECKFORD, I. B. C., M.B. Edin., D.P.H.: assistant M.O.H., Greenlock.
WILLCOX, D. R. C., M.B. Lond.: consultant pathologist, Bethlem Royal Hospital and the Maudsley Hospital, London.

Diary of the Week

SEPT. 22 TO 28

Tuesday, 24th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, London, W.C.2
5 P.M. Prof. George Wald: The Molecular Basis of Vision. (Edridge Green lecture.)

Thursday, 26th

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. J. Francis Silva (Colombo): Old Dislocations of the Elbow. (Hunterian lecture.)
FOUNTAIN HOSPITAL, Tooting Grove, S.W.17
5.30 P.M. Prof. R. S. Illingworth, Dr. Ruth Griffiths: Early Diagnosis of Mental Deficiency.

Friday, 27th

INSTITUTE OF PSYCHIATRY
3 P.M. (Maudsley Hospital, Denmark Hill, S.E.5.) Prof. Leo Kanner (Baltimore): Sources and Results of Perfectionism in Child Rearing.
BRITISH TUBERCULOSIS ASSOCIATION
11.15 A.M. *With the Midland Thoracic Society.* (Medical School, Edgbaston, Birmingham, 15.) Dr. C. H. C. Toussaint: Prevention of the Common Pulmonary Diseases. (Presidential address; opening of two-day meeting.)

Saturday, 28th

ASSOCIATION OF CLINICAL BIOCHEMISTS
9.30 A.M. *With the Association of Clinical Pathologists.* (Royal College of Surgeons.) Scientific meeting.

Notes and News

THE NATIONAL FORMULARY

THE systematic use of the *National Formulary*, now called the *British National Formulary*, pays handsome dividends in time and trouble saved. In the new edition [1] there are over 100 additions to the formulary proper, but 67 items which appeared in the 1955 edition have been deleted and the composition of 23 others has been amended. The book would be an acquisition for its index alone which lists some 2000 items. Complementary to the ordinary alphabetical index, there is now a pharmacological classification, and it will be interesting to know what reception it gets from general practitioners. If the classification is not used, it will be hard to justify its retention, for it adds 16 pages to the *Formulary*. There is little doubt that the pharmacological classification will interest students; and their needs are met even more generously by the alternative edition, costing a shilling more, which is based on a pharmacological classification and contains brief notes on the actions of many of the drugs.

The lists of proprietary preparations and the equivalent drugs are invaluable, though not, of course, complete; and the appendix also includes the useful Dental Practitioners' Formulary and helpful tables on metric and imperial doses.

Students will also continue to value the Notes for Prescribers for the explicit advice they offer on the treatment of common diseases. The notes have been extended to include short sections on agricultural poisons, dangerous drugs, and schedule-IV poisons. After Poisoning, the notes are arranged alphabetically, which is perhaps a pity since, from a clinical viewpoint, the presentation becomes higgledy-piggledy. Occasional words and phrases are less clear and terse than is desirable in a book of this kind. But these are small criticisms of an extremely successful enterprise.

NIGHT VISITS TO CANCER PATIENTS

DURING the next six months the Marie Curie Memorial Foundation is to try the experiment of offering nursing care to cancer patients who are being looked after in their homes.

This pilot scheme, which will begin on Oct. 2, will be limited to patients living in the London postal areas of N.W.3, N.W.5, and N.W.6. Two nurses, with district-nursing qualifications, will be available; and it is intended that patients should receive, according to their needs, one or two visits during the night for injections, dressings, or nursing care. The service will not be available for night-sitting or domestic needs. No fees will be charged during the test period, but donations may be sent to the foundation. The service is not available to families able to pay for night nursing; but sympathetic consideration will be given to cases where the family, though willing to pay for a night nurse, is unable to obtain one, or needs this help for a brief period while arrangements for a night nurse are being made.

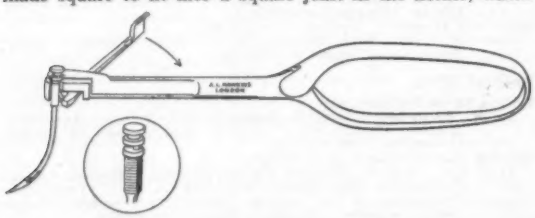
The two visiting nurses will be based at the foundation's home at Edenhall, 11, Lyndhurst Gardens, N.W.3, to which requests for this service should be made by the patient's doctor.

MODIFICATION OF BONNEY-REVERDIN NEEDLEHOLDER

Mr. BRAITHWAITE RICKFORD writes:

For a long time the Bonney-Reverdin needleholder has proved unsatisfactory. The modification shown in the accompanying figure includes an alteration to the head of the needle and the socket of the holder.

In the past, this joint has been made round, and, after considerable wear, there has been a tendency for the needle to slip in the holder. The head of the needle has now been made square to fit into a square joint in the holder, which will overcome the tendency to rotation. With this modification the needle can be placed in three stable positions.



The instrument has been made by Messrs. A. L. Hawkins & Co., 15, New Cavendish Street, London, W.1.

1. British National Formulary, 1957. London: British Medical Association and Pharmaceutical Press. 1957. Standard edition. Pp. 226. 6*s*. 6*d*. Alternative edition. Pp. 245. 7*s*. 6*d*. Interleaved copies are available at 10*s*. and 10*s*. 6*d*. respectively.

Royal College of Physicians of Edinburgh

Dr. W. Ritchie Russell will deliver the Morison lecture on Thursday, Oct. 24. His subject will be the physiology of learning. Sir Russell Brain will deliver the Frederick Price lecture on Thursday, Nov. 14. He will speak on neurology—past, present, and future. Both lectures will be at the college, 9, Queen Street, Edinburgh 2, at 5 P.M.

Royal College of Obstetricians and Gynæcologists

A memorial service for the late president, Sir Charles Read, will be held in All Souls Church, Langham Place, London, W.1, on Friday, Sept. 27, at 11.45 A.M.

Royal Air Force Appointment

Air Commodore James Hill has been appointed principal medical officer at Home Command with the acting rank of air vice-marshal.

Society of Apothecaries of London

On Thursday, Oct. 10, at 5.30 P.M., in the Apothecaries' Hall, Black Friars Lane, E.C.4, Dr. Maurice Campbell will deliver the Joseph Strickland Goodall lecture. His subject will be the results of surgical treatment in congenital heart disease.

King's College Hospital

On Friday, Oct. 4, at 4.30 P.M., in the medical school, Denmark Hill, London, S.E.5, Sir Cecil Wakeley will give the Thomas Percy Legg lecture. He is to speak on external herniæ.

Royal Free Hospital School of Medicine, London

On Friday, Oct. 4, at 3 P.M., in the Senate House, University of London, W.C.1, Mr. Justice Lloyd-Jacob will give the inaugural address of the session, when his subject will be Responsibility.

Institute of Dermatology, London

The first semi-permanent exhibition of the winter course, by Dr. C. D. Calnan, Dr. H. Haber, and Dr. G. C. Wells on pigmented lesions of the skin, will be open from Oct. 1 to 20 at the institute, Lisle Street, W.C.2.

British Postgraduate Medical Federation

On Thursday, Oct. 17, at 5.30 P.M., at the Senate House, University of London, Malet Street, W.C.1, Mr. Julian Huxley, D.SC., F.R.S., will deliver the first lecture of the 1957–58 series on the scientific basis of medicine. His subject will be, some biological aspects of cancer.

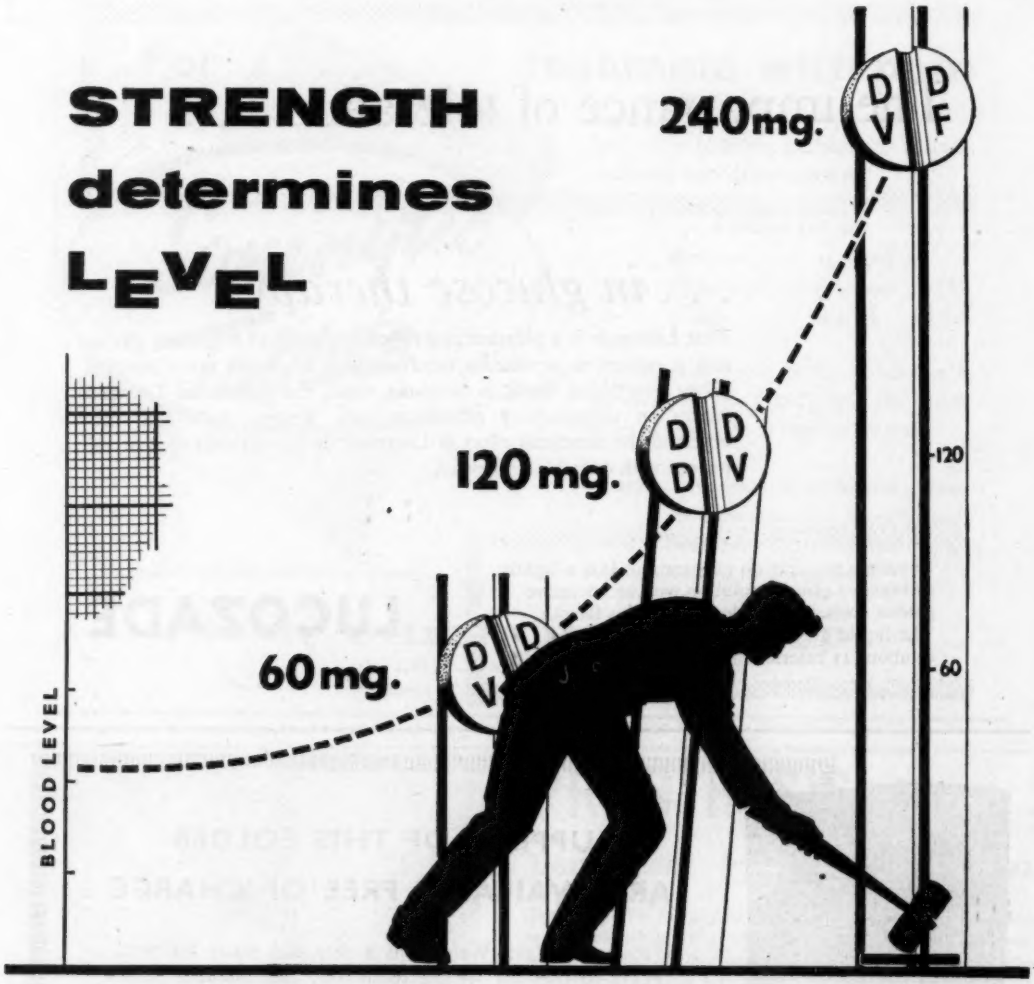
Marlborough Day Hospital

The lectures given at this hospital, on the first Monday of each month, for doctors and professional people working in the mental-health field, will recommence on Monday, Oct. 7, at 8.15 P.M. Further particulars may be had from the medical director of the hospital, 38, Marlborough Place, St. John's Wood, London, N.W.8.

Psychiatric Films from France

On Thursday, Oct. 17 at 6.30 P.M., at the Mezzanine Cinema, Shell Mex House, Strand, London, W.C.2, the following films will be shown: Antoine et les élémentaux ou la pensée magique d'un paraphrène (made by Dr. Bobon and Dr. Verdeaux, introduced by Dr. E. B. Strauss); L'Univers plastique des schizophrènes (Dr. Volmat, introduced by Dr. G. M. Carstairs); Réaction, automatisme, activité rythmique du nouveau-né et du nourrisson (Mlle S. Autgaerden and Dr. André Thomas; discussion to be led by Dr. Portia Holman); Pharmacologie psychiatrique (Dr. Thuillier, introduced by Dr. L. C. Cooke); Crises psychomotrices provoquées chez les épileptiques temporaux (Professor Gastaut, introduced by Dr. D. A. Pond). Admission will be free. Further particulars may be had from the scientific bureau of the French Embassy, 22, Wilton Crescent, S.W.1.

CORRIGENDUM: *Students' Guide*.—On p. 440 (Aug. 31), under Dublin, in the postgraduate section of the Guide, we said that the diploma in public health was temporarily in abeyance. We should have made it clear that we were referring to the diploma of the University of Dublin. A course for the diploma in public health of the National University of Ireland is in fact held each year at University College, Dublin.



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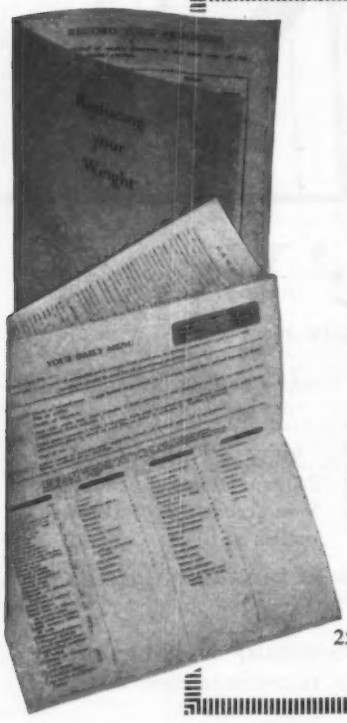

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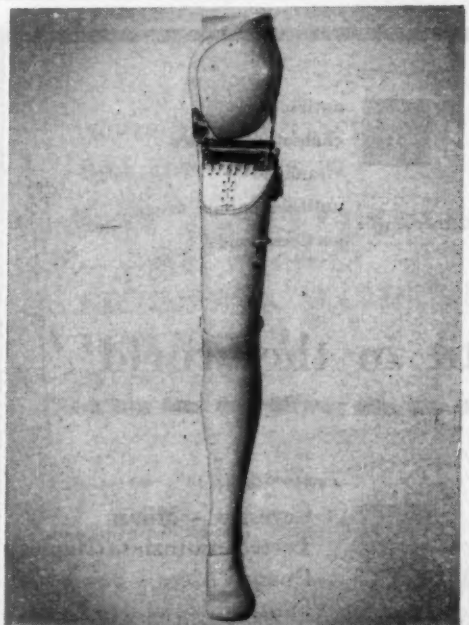

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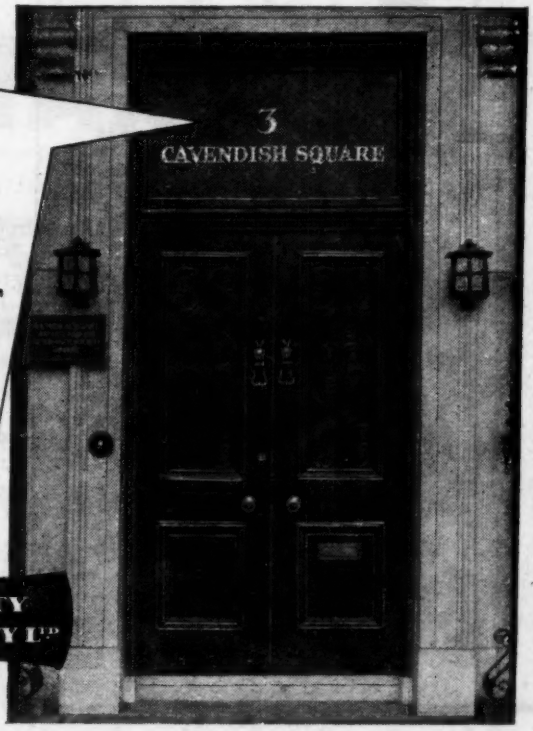

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The fee for attending either of these courses is 2 guineas.

Application for a ticket should be made to The Dean, Institute of Neurology (Queen-square), The National Hospital, Queen-square, W.C.1, and a remittance to cover the fee enclosed. Only postal applications will be considered.

UNIVERSITY OF LONDON

A LECTURE entitled "Circulatory Complications of Improper Respiration During General Anæsthesia" will be delivered by Prof. E. M. PAPPER (Columbia University) at 5.30 P.M. on 1ST OCTOBER at the Westminster Medical School (Meyerstein Lecture Theatre), Horseferry-road, S.W.1.

Admission free, without ticket.

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A SHORT INTENSIVE COURSE in the PRACTICE OF INDUSTRIAL MEDICINE will be held in the Department of Occupational Health, Manchester University, commencing MONDAY, 28TH OCTOBER to SATURDAY, 2ND NOVEMBER, inclusive. Numbers will be strictly limited. Registration fee £7 7s.

Applications should be sent to the Secretary, Nuffield Department of Occupational Health, Clinical Sciences Building, York-place, Manchester, 13, from whom further particulars may be obtained.

UNIVERSITY OF MANCHESTER
FACULTY OF MEDICINE

A REFRESHER COURSE for General Practitioners will be held in conjunction with the North-West England Faculty of the College of General Practitioners. LECTURE DEMONSTRATIONS will be given in the Clinical Sciences Building, York-place, Manchester, 13, on alternate SUNDAY mornings from 11 a.m. till 12 NOON, commencing on 6TH OCTOBER and concluding on 15TH DECEMBER, 1957. The instruction will be given by Senior members of the teaching staff of the Manchester Royal Infirmary.

Particulars of the Course may be obtained from the Dean of Postgraduate Medical Studies, The University, Manchester, 13. There will be no fee for the course.

UNIVERSITY COLLEGE LONDON (Gower-street, W.C.1)

Prof. M. HEIDELBERGER (Institute of Microbiology, Rutgers, U.S.A.) will give a PUBLIC LECTURE entitled "The Chemistry of Proteins and Carbohydrates in Relation to Immunological Specificity" on TUESDAY, 1ST OCTOBER, at 5 P.M.

Admission free, without ticket.

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Prospectuses, enrolment forms, and full details may be obtained from the Acting Secretary, 28, Portland-place, London, W.1 (Telephone: LANgham 2731/2).

INSTITUTE OF ACCIDENT SURGERY
(In conjunction with the Board of Graduate Studies, The Medical School, University of Birmingham)

A 3-DAY COURSE on BURNS will be held at Birmingham Accident Hospital from TUESDAY to THURSDAY, 5TH–7TH NOVEMBER, 1957.

PROGRAMME

Tuesday, 5th November
9.00 A.M. .. Introduction by Mr. WILLIAM GISSANE.
9.30 A.M. .. The Treatment of Shock.
11.30 A.M. .. Primary Excision and Grafting.
2.00 P.M. .. The Control of Infection.
Wednesday, 6th November
9.30 A.M. .. Delayed Grafting and Associated Problems.
11.30 A.M. .. Contractures.
2.00 P.M. .. Demonstrations—
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Blood volume techniques.
Control of infection.
Pathological specimens.
Skin respirometry.
Thursday, 7th November
9.30 A.M. .. Causes of Death from Burning.
11.30 A.M. .. Social and Psychological Problems associated with Burns.
2.00 P.M. .. Discussion.

Lecturers will include Dr. J. P. BULL, Mr. D. M. JACKSON, Dr. E. J. L. LOWBURY, Dr. ELIZABETH TOPLEY and Dr. S. SEVITT.

The Course is intended for Surgeons, Registrars and others concerned with the treatment of burns at the acute stage.

The fee (including lunch and tea) is 4 guineas.

Applications should be made to the Secretary, Institute of Accident Surgery, Birmingham Accident Hospital, Bath-row, Birmingham, 15.

PRIMARY F.F.A.R.C.S.
DECEMBER, 1957

A COURSE of EVENING TUTORIALS in ANATOMY, PHYSIOLOGY, and PHARMACOLOGY will be held at Lambeth Hospital, S.E.11 (Elephant and Castle), during OCTOBER and NOVEMBER.

For details apply Secretary, Department of Anæsthesia, Lambeth Hospital, S.E.11.

NATIONAL HEART HOSPITAL
Westmoreland-street, W.1, and Buckingham

The ST. CYRES LECTURE for 1957 will be delivered in the Barnes Hall of the Royal Society of Medicine, 1, Wimpole-street, W.1, on TUESDAY, 15TH OCTOBER, at 5 P.M., by Dr. A. RAE GILCHRIST.

Subject: Clinical Aspects of High Grade Heart Block.

Members of the Medical Profession are cordially invited.

EMPIRE RHEUMATISM COUNCIL. Applications are invited for 2 TRAVELLING FELLOWSHIPS in 1958 tenable for up to 1 year, to prosecute research on some aspect of the Rheumatic Diseases. Medical or scientific qualifications are required. Salary according to qualifications and experience, but not less than £1000 p.a. (for lesser period than 1 year, pro rata).

Applications, stating age, qualifications and experience, should be sent in triplicate, with the names of 2 referees, not later than 1st October, 1957, to the A/General Secretary, Empire Rheumatism Council, Faraday House, 8/10, Charing Cross-road, London, W.C.2.

ROYAL FREE HOSPITAL SCHOOL OF MEDICINE, 8, Hunter-street, W.C.1. Part-time medically qualified RESEARCH ASSISTANT required from October. Salary approximately £350 p.a.

Inquiries to the Secretary.

THE UNIVERSITY OF MANCHESTER. Applications are invited for the post of LECTURER or ASSISTANT LECTURER in the Clinical Section of the Rheumatism Research Centre. Salary: Lecturer, on a scale rising to £2150 p.a.; Assistant Lecturer, £900–£100–£1300 p.a. Status and initial salary according to qualifications and experience. Membership of the F.S.S.U. and children's allowance scheme.

Applications should be sent not later than 1st October, 1957, to the Registrar, the University, Manchester, 13, from whom further particulars and forms of application may be obtained.

THE QUEEN'S UNIVERSITY OF BELFAST invites applications for a LECTURESHIP IN PHYSIOLOGY, consequent upon the appointment of Dr. R. F. WHELAN to the Chair of Physiology in the University of Adelaide. The vacancy will occur in January, 1958, and it is desired to fill it as soon as possible and not later than October, 1958. The salary will be in the range of £1300–£50–£2100 with provisions for superannuation. Initial placing on the salary scale will depend upon experience and qualifications. In certain circumstances the salary may rise to £2250.

Applications should be submitted not later than 15th November, 1957. Further particulars may be obtained from the Secretary of the University.

AUSTRALIA. UNIVERSITY OF ADELAIDE. Medical SCHOOL. The University invites applications for the following newly established posts.

(1) PROFESSOR OF SURGERY.
(2) PROFESSOR OF OBSTETRICS AND GYNÆCOLOGY.
(3) READER IN MEDICINE.

The Professors and the Reader will be stationed at the Queen Elizabeth Hospital, a new hospital of some 300 Beds, in which both office and laboratory accommodation for the University Departments is being provided.

The basic salary attached to each Chair will be £A3000, with a special allowance of £A500 a year; the salary scale for a Reader is £A2200–£A50–£A2400, with a special allowance for this post of £A200 a year. Superannuation on the F.S.S.U. basis will be provided on the basic salaries; and the Professors will be able to engage in a limited amount of private consultant practice on conditions approved by the Council.

Potential candidates are invited to obtain from the Secretary, Association of Universities of the British Commonwealth, 36, Gordon-square, London, W.C.1, or from the Registrar, a general statement about these posts and formal terms of appointment in each case. Those in the United Kingdom may also borrow from the Secretary, A.U.B.C., a coloured film illustrating the University and the city of Adelaide.

Particulars of a scheme for financial help in the purchase of a house may be obtained from the Registrar; and the University will gladly supply further information on request.

Applications (in duplicate), giving the information specified in the general statement, should reach the Registrar, University of Adelaide, Adelaide, South Australia, not later than 31st October, 1957.

Hospital Services: Senior Appointments

ROYAL MASONIC HOSPITAL, Ravenscourt Park, London, W.6. Applications are invited from Fellows of one of the Royal Colleges of Surgeons for the appointment of CONSULTANT THORACIC SURGEON at the above Hospital as from on or about 1st January, 1958. Candidates must be engaged in consulting practice and well established in their profession.

Applications, giving detailed information and the names and addresses of 3 referees, should reach the undersigned (from whom further information may be obtained) on or before 12th October, 1957. R. E. LAWSON, Secretary and House Governor.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Whole-time CONSULTANT GERONTOLOGIST. Duties mainly at Cross Houses Hospital, Shrewsbury and peripheral hospitals in Salop area. Wide experience specialty/higher qualification essential.

Applications (15 copies), stating name, age, nationality, present and previous appointments and details of 3 referees, to Secretary, 10, Augustus-road, Birmingham, 15, by 21st October.

BIRMINGHAM REGIONAL HOSPITAL BOARD. St. GEORGES HOSPITAL, STAFFORD. Whole-time CONSULTANT PSYCHIATRIST AND DEPUTY MEDICAL SUPERINTENDENT. Duties also at Coton Hill Hospital and associated clinics. House provided. D.P.M./wide experience specialty essential.

Applications (15 copies), stating name, age, nationality, present and previous appointments and details of 3 referees, to Secretary, 10, Augustus-road, Birmingham, 15, by 21st October.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Stoke-ON-TRENT GROUP OF HOSPITALS. Whole-time CONSULTANT PHYSICIAN (geriatrics) responsible for organisation and control of geriatric services within the Group. Duties at City General Hospital where geriatric unit is to be established and at 6 other hospitals where geriatric beds are available. Higher qualification and wide experience geriatrics essential.

Applications (15 copies), stating name, age, nationality, present and previous appointments and details of 3 referees, to Secretary, Regional Hospital Board, 10, Augustus-road, Birmingham, 15, by 21st October.

MANCHESTER REGIONAL HOSPITAL BOARD. Bury AND ROSSENDALE AND ROCHDALE AND DISTRICT HOSPITAL MANAGEMENT COMMITTEES. Locum CONSULTANT RADIOLOGIST (maximum part-time) required immediately for the above Hospital Centres, for approximately 2 months. Salary according to individual status.

Apply, stating full details to—
H. WILKINSON, Group Secretary.
Bury General Hospital, Bury, Lancs.

MANCHESTER REGIONAL HOSPITAL BOARD. Whole-time or maximum Part-time CONSULTANT PSYCHIATRIST to Lancaster Moor (Mental) Hospital (2500 Beds) and to the Royal Lancaster Infirmary and the Queen Victoria Hospital, Morecambe, where outpatient clinics will be conducted. The Consultant appointed will be designated Medical Superintendent of Lancaster Moor Hospital and could be resident there. If not resident, he will be required to live near to the Hospital. All forms of modern therapy are undertaken. Applicants must be of high professional standing with wide experience and possess higher qualifications.

Requests for application forms should be made to the Board's Senior Administrative Medical Officer, Cheetwood-road, Manchester, 8, and completed forms should be returned by 7th October, 1957.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

Full or maximum Part-time CONSULTANT in Orthopædic and Traumatic Surgery to Romford Group of hospitals, based on Oldchurch Hospital, Romford, Essex. Residence in Group area a condition of appointment. Further particulars on application.

Part-time CONSULTANT SURGEON to W. J. Courtauld Hospital, London-road, Braintree, Essex, for 2 sessions a week.

Applications (6 copies), stating post concerned, and names of 3 referees, should reach the Secretary, 11A, Portland-place, London, W.1, by Saturday, 19th October.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.

(1) CONSULTANT PSYCHIATRIST (whole-time), St. Bernard's Hospital, Southall, Middlesex (2507 Beds). Accommodation available for single candidate.

Applications before 21st October, 1957.

(2) CONSULTANT PSYCHIATRIST (whole-time), Hill End Hospital, St. Albans, Herts (692 Beds).

Applications before 24th October, 1957.

Hospitals may be visited by direct appointment.

Application forms obtainable from, and returnable to, Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1.

OXFORD REGIONAL HOSPITAL BOARD. Consultant in Anæsthetics (whole-time or maximum part-time) to the hospitals of the Reading Hospital Management Committee. Applicants must hold the F.F.A.R.C.S. and have had wide experience in anæsthetics. The successful candidate will be required to live in the Reading area. Applicants may visit the hospitals by arrangement with the Hospital Management Committee Secretary.

Applications (9 copies), stating age, qualifications, experience, and the names of 3 referees, must reach the Secretary of the Board, 43, Banbury-road, Oxford, by 22nd October.

SHEFFIELD REGIONAL HOSPITAL BOARD. Maximum Part-time CONSULTANT GENERAL SURGEON required. Duties in hospitals in the Leicester Area.

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Sheffield, 10. Forms to be returned by 19th October, 1957.

SHEFFIELD REGIONAL HOSPITAL BOARD. Maximum Part-time CONSULTANT RADIOLOGIST required. Duties mainly in hospitals in the Mansfield Area.

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 19th October, 1957.

SCOTLAND. NORTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the post of Whole-time CONSULTANT SURGEON in the Shetland Islands. Candidates should have comprehensive surgical experience. Principal duties are at the Gilbert Bain Hospital, Lerwick, where the officer to be appointed will be in charge of surgical beds. Construction of a new hospital is about to start. A residence convenient to the Hospital is available. Terms and conditions of service are as laid down for appointment to hospital medical and dental staffs under the National Health Service (Scotland) Act.

Applications, together with the names of 2 referees, should be forwarded by 12th October to the Senior Administrative Medical Officer, 1, Albyn-place, Aberdeen, from whom further particulars and a form of application may be obtained.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of ASSISTANT E.N.T. SURGEON at the Glasgow Ear, Nose and Throat Hospital and Glasgow School Clinics. The appointment will be part-time on the basis of 9 sessions per week. Salary (at age 32 and over) on the scale £1653 15s.–£52 10s.–£2126 5s.

Applications (16 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, not later than 30 days after the publication of this advertisement.

WELSH REGIONAL HOSPITAL BOARD. Consultant RADIOLOGIST, West Wales Hospital Management Committee. Based at West Wales General Hospital, Carmarthen, with visits to other hospitals in group. Vacant July, 1958. Optional whole-time/maximum part-time appointment.

Applications (12 copies), naming 3 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 21 days.

WELSH REGIONAL HOSPITAL BOARD. Whole-time ASSISTANT RADIOLOGIST (Senior Hospital Medical Officer) to serve the Caernarvon and Anglesey Hospital Management Committee, based at Caernarvon and Anglesey General Hospital, Bangor, with visits to other hospitals in the Group.

Applications (12 copies), naming 3 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 21 days.

WELSH REGIONAL HOSPITAL BOARD. Whole-time SENIOR CASUALTY OFFICER required at Caerphilly District Miners' Hospital, in the Rhymney and Sirhowy Valleys Hospital Management Committee area. Vacant on 1st January, 1958. Commodious family flat at reasonable rent. Salary within range of £1653 15s.–£2126 5s. Tenure of appointment for a period not exceeding 4 years.

Applications (12 copies), naming 3 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 21 days.

SYDNEY. ROYAL SOUTH SYDNEY HOSPITAL, Joynton-avenue, ZETLAND, SYDNEY, AUSTRALIA. (Acute Hospital of 100 Beds.) Applications are invited from registered medical practitioners for the position of MEDICAL SUPERINTENDENT at the above Hospital, situated in a large industrial area. Total attendances Casualty and Outpatients Department —61,000 per year. Accommodation available at the Hospital for a single man. Salary in accordance with determination approved by the Hospitals Commission of N.S.W., at present, £A2014 p.a., less £188 a year for board and residence.

Applications endorsed "Medical Superintendent," stating age, qualifications, experience, nationality and marital status together with copies of 3 testimonials, to be forwarded to reach the undersigned not later than 1st October, 1957. The successful applicant will be required to commence duties during January, 1958.

R. T. WRIGHT,
Secretary and Chief Executive Officer.

Hospital Services : Junior Appointments

ACTON HOSPITAL, Gunnersbury-lane, W.3. Senior HOUSE OFFICER (resident) required from 1st October, 1957, for inpatient duties ; mixed specialties.

Applications to Hospital Secretary within 7 days.

BROMPTON HOSPITAL, S.W.3. Applications invited for the post of NON-RESIDENT HOUSE PHYSICIAN for which there are 2 vacancies for 6 months from 1st December, 1957. Duties include work in Outpatient Department and wards. Salary at the rate of £557 10s. p.a.

Applications, stating age, qualifications with dates, nationality, and appointments held, together with copies of testimonials, by 5th October, 1957, to—

KENNETH A. F. MILES, House Governor.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. RESIDENT HOUSE OFFICER required in General Medical Department, including hæmatology and endocrinology. Post-registration appointment for 6 months from 1st November, 1957.

Applications, with 2 testimonials, to Medical Director by 28th September, 1957. Please submit separate applications for each post and state clearly for which position you are applying.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. RESIDENT HOUSE OFFICER required in General Medical and Neurological Department. Post-registration appointment for 6 months from 9th November, 1957.

Applications, with 2 copy testimonials, to Medical Director by 28th September, 1957. Please submit separate applications for each post and state clearly for which position you are applying.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. RESIDENT HOUSE OFFICER required in General Medical and Cardiological Department (post- or pre-registration). Post vacant 17th November, 1957.

Applications, with 2 testimonials, to Medical Director by 28th September, 1957. Please submit separate applications for each post and state clearly for which position you are applying.

CONNAUGHT HOSPITAL, Walthamstow, E.17. (123 Beds.) Applications are invited for the post of SECOND CASUALTY OFFICER with duties in the Department of Orthopædic and Traumatic Surgery (Senior House Officer grade). Recognised for F.R.C.S. Salary £819 10s. p.a., less £150 p.a. for board, lodging, &c.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

EAST END MATERNITY HOSPITAL, 384/398, Commercial-road, London, E.1. (58 Beds.) RESIDENT OBSTETRICAL OFFICER (Senior House Officer grade). Recognised for M.R.C.O.G. Post vacant 1st November, 1957.

Applications, with copies of not more than 3 testimonials, to be sent to the Secretary, Stepney Group Hospital Management Committee, Mile End Hospital, Bancroft-road, London, E.1, not later than 24th September, 1957.

ELIZABETH GARRETT ANDERSON HOSPITAL, Euston-road, N.W.1. (ROYAL FREE HOSPITAL GROUP.) Applications are invited from pre-registration and registered Women medical practitioners for the post of HOUSE SURGEON to Gynæcological Department (recognised for M.R.C.O.G.). Duties to commence 1st November, 1957. Appointment for 6 months. Salary in accordance with Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, Elizabeth Garrett Anderson Hospital, by 25th September, 1957.

KING EDWARD MEMORIAL HOSPITAL, Ealing, SOUTH WEST MIDDLESEX HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER to General Surgeon with some E.N.T. duties. Preference given to persons seeking pre-registration post.

Applications, stating age, nationality, qualifications with dates, and experience, together with copies of 2 recent testimonials, to Group Secretary, West Middlesex Hospital, Isleworth, by 30th September, 1957.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. Applications are invited for the appointment of RESIDENT MEDICAL OFFICER. Appointment for 1 year from 1st December, 1957, and graded as Registrar.

Applications, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should be sent to the undersigned not later than 12th October.

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

LONDON JEWISH HOSPITAL, Stepney Green, E.1. (130 Beds.) HOUSE SURGEON (pre- or post-registration) required for 6 months. Post vacant immediately.

Applications, stating age, experience, &c., and copies of not more than 3 testimonials, to be sent to the Hospital Secretary not later than 27th September, 1957.

NATIONAL HOSPITALS FOR NERVOUS DISEASES. Applications are invited for the full-time appointment of MEDICAL REGISTRAR (non-resident) at Maida Vale Hospital for Nervous Diseases, London, W.9. Grading as Senior Registrar. Preference will be given to a candidate holding a higher degree who intends to specialise in neurology.

Applications, with copies of 3 recent testimonials, to be sent to the Secretary at Maida Vale Hospital, not later than 2nd October, 1957.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

GERIATRIC REGISTRAR (resident or non-resident), St. Matthew's Hospital, Shepherdess-walk, London, N.1 (320 Beds).

ANÆSTHETIC REGISTRAR (resident or non-resident), St. Andrew's Hospital, Billericay, Essex. Recognised for F.F.A.R.C.S.

ANÆSTHETIC REGISTRAR (non-resident, sleeping in on duty nights), Chase Farm Hospital and other hospitals in the Enfield Group, Enfield, Middlesex. Recognised for D.A. and F.F.A.R.C.S. Post affords wide practical experience under Consultant supervision.

MEDICAL REGISTRAR (resident or non-resident, sleeping in on duty nights), Hackney Hospital, Homerton High-street, E.9.

MEDICAL REGISTRAR (resident or non-resident), German Hospital, Dalston-lane, E.8.

REGISTRAR in Obstetrics and Gynæcology (resident or non-resident), Oldchurch Hospital, Romford, Essex (88 obstetric and 52 gynæcological beds). Recognised for M.R.C.O.G.

REGISTRAR in Diseases of the Chest (resident; married quarters available), Harts Hospital, Woodford Green, Essex. Previous experience of chest diseases and tuberculosis essential.

Appointments subject to review after 1 year.

Application forms from Secretary, 11a, Portland-place, W.1, to be returned by 5th October.

NORTH LONDON BLOOD TRANSFUSION CENTRE, Deansbrook-road, EDGWARE, MIDDLESEX. JUNIOR HOSPITAL MEDICAL OFFICER for full-time duties with mobile teams at donor sessions. The appointment is for 3 years. Vacant 1st October, 1957.

Applications, giving age, qualifications, experience, and names of 2 referees, to Director not later than 28th September, 1957.

NORTH MIDDLESEX HOSPITAL, Edmonton, N.18. RESIDENT HOUSE SURGEON (general, orthopædic and traumatic surgery), pre- or post-registration, required for 6 months, starting 1st November. Post recognised for F.R.C.S.

Applications, stating age, nationality, qualifications, experience, with copies of recent testimonials, to Secretary of Hospital, by 2nd October.

NORTH MIDDLESEX HOSPITAL, Edmonton, N.18. 2 OBSTETRIC AND GYNÆCOLOGICAL HOUSE SURGEONS (resident) required for 1st November.

(*a*) Post-registration.

(*b*) Pre-registration (second post).

Both posts recognised by R.C.O.G. for Diploma, and as a combined post for Membership. Candidates must have held house appointments in either medicine or surgery. Large Obstetric and Gynæcological Department.

Applications (in own handwriting), stating age, nationality, qualifications, experience, with copies of recent testimonials, to Secretary of Hospital, by 2nd October.

PUTNEY HOSPITAL, Lower Common, S.W.15. Casualty OFFICER AND E.N.T. HOUSE SURGEON, vacant 1st November, 1957. Non-resident. Senior House Officer grade. Recognised F.R.C.S.

Apply Hospital Secretary, enclosing copies of 3 recent testimonials, not later than 30th September, 1957.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, E.15. JUNIOR CASUALTY OFFICER (House Officer third post) required for 6 months as soon as possible.

Applications, with the names of 3 referees, to the Hospital Secretary by 4th October, 1957.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, E.15. PÆDIATRIC HOUSE PHYSICIAN (Male or Female: House Officer, third post). Duties will include some work in related departments (e.g., Diabetic Clinic, &c.). 6 months appointment commencing 14th October, 1957, approximately. Post recognised for D.C.H.

Applications, with the names of 3 referees, to Hospital Secretary by 28th September, 1957.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, E.15. SENIOR OBSTETRIC HOUSE SURGEON (Male or Female: Senior House Officer grade). 6 months commencing 1st November, 1957. Post recognised for M.R.C.O.G.

Applications, with the names of 3 referees, to Group Secretary, West Ham Group Hospital Management Committee, Stratford, E.15, by 28th September, 1957.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, E.15. OBSTETRIC HOUSE SURGEON (Male or Female: House Officer, third post). 6 months commencing 1st November, 1957. Successful candidate may be eligible for appointment as Senior Obstetric House Surgeon (Senior House Officer grade) for the following 6 months. Post recognised for M.R.C.O.G.

Applications, with the names of 3 referees, to Hospital Secretary by 28th September, 1957.

QUEEN ELIZABETH HOSPITAL FOR CHILDREN MANAGEMENT COMMITTEE, Hackney-road, E.2, Shadwell, E.1, and BANSTEAD WOOD, SURREY. SENIOR RESIDENT MEDICAL OFFICER (Male or Female), graded Senior House Officer—senior of 7 House Officers in a hospital engaged in postgraduate and undergraduate teaching. Previous pædiatric experience essential. Post vacant 1st November, 1957, at Hackney-road branch. Appointment for 1 year.

Application forms (obtainable from the Secretary at Hackney-road), should be returned with copies of 3 testimonials before 27th September, 1957.

QUEEN ELIZABETH HOSPITAL FOR CHILDREN MANAGEMENT COMMITTEE, Hackney-road, E.2, Shadwell, E.1, and BANSTEAD WOOD, SURREY. SENIOR RESIDENT MEDICAL OFFICER (Male or Female), graded Senior House Officer—previous pædiatric experience essential. Post vacant 1st November, 1957, at the Hospital's country branch at Banstead. Appointment for 1 year.

Application forms (obtainable from the Secretary at Hackney-road) should be returned with copies of 3 testimonials before 27th September, 1957.

ROYAL NATIONAL ORTHOPÆDIC HOSPITAL, 234, Great Portland-street, London, W.1. Applications are invited for the appointment of ORTHOPÆDIC REGISTRAR (full-time), non-resident (2 vacancies). Preference will be given to candidates with a higher surgical qualification. Duties to commence 1st November, 1957, and 10th December, 1957, respectively.

Applications to be received not later than 28th September. Forms of application can be obtained from the House Governor at 234, Great Portland-street, London, W.1.

ROYAL NATIONAL ORTHOPÆDIC HOSPITAL, BROCKLEY HILL, STANMORE, MIDDLESEX. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER (2 vacancies) for a period of 6 months. Duties to commence on 30th November and 11th December, 1957.

Applications to be received by 14th October, 1957. Forms of application can be obtained from the House Governor at 234, Great Portland-street, London, W.1.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in General Surgery (resident) to fill a vacancy in the approved trainee establishment at the Seamen's Group of hospitals, for duty mainly at the Dreadnought Seamen's Hospital, Greenwich, S.E.10. Married quarters may be available. The appointment, which will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance, is available on 2nd December, 1957.

Applications, giving particulars of age, qualifications, and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 5th October, 1957.

SOUTH-EAST REGIONAL THORACIC SURGERY UNIT. (50 Beds.) BROOK GENERAL HOSPITAL, Shooters Hill-road, S.E.18. SENIOR HOUSE OFFICER, vacant 1st November. Recognised for F.R.C.S. 6 months appointment and may then be renewed for a further period. The Unit treats all types of chest diseases and offers opportunity for comprehensive training in thoracic surgery.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

SPRINGFIELD HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required. The Hospital is a large one and offers excellent experience in diagnosis and treatment of all forms of mental disorders including the neuroses. Every variety of modern treatment is carried out in a well-equipped treatment centre. Single accommodation is available. Candidates may visit the Hospital by arrangement.

Apply Group Secretary, Springfield Hospital, Tooting, S.W.17, for application forms which should be returned duly completed on or before 5th October, 1957.

ST. JAMES' HOSPITAL, Balham, London, S.W.12. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SURGICAL REGISTRAR required. Post vacant October. Applicants should possess F.R.C.S.

Application forms, obtainable from Group Secretary, Wandsworth Hospital Group, at above address, to be completed and returned by 5th October. (0609.)

ST. JAMES' HOSPITAL, Balham, London, S.W.12. South West Metropolitan Regional Hospital Board. E.N.T. REGISTRAR (resident).

Application forms obtainable from Group Secretary, Wandsworth Hospital Group, at above address. (0400.)

ST. GILES' HOSPITAL, Camberwell, S.E.5. House SURGEON (casualty duties, with some general surgical, E.N.T. and eye beds). Recognised pre-registration post.

Applications, with copy testimonials or names of referees, to Group Secretary, Camberwell Hospital Management Committee, Dulwich Hospital, East Dulwich-grove, S.E.22.

ST. LEONARD'S HOSPITAL, Nuttall-street, London, N.1. (General—192 Beds.) Applications are invited from registered or provisionally registered medical practitioners for the post of HOUSE PHYSICIAN for 6 months commencing 7th October, 1957.

Applications, with 2 recent testimonials, to be sent to the Hospital Secretary, by 27th September, 1957.

ST. MARY ABBOTS HOSPITAL, Marloes-road, Kensington, W.8. SENIOR HOUSE OFFICER (Casualty Officer) resident or non-resident. Post vacant 1st November, 1957. Post recognised for F.R.C.S. (Eng.). Candidates may visit the Hospital by arrangement with the Surgeon-Superintendent.

Applications by 30th September, 1957, on forms obtainable from the Hospital Secretary. (L.87.)

ST. MARY ABBOTS HOSPITAL, Marloes-road, Kensington, W.8. Applications are invited for appointment as REGISTRAR in Anæsthetics. Position based at St. Mary Abbots Hospital, but expected to work at other hospitals in the Group if required. Post recognised for the D.A. and application has been made for recognition for the F.F.A.R.C.S. Resident on nights on duty. Candidates may visit the Hospital by arrangement.

Applications (5 copies), to be submitted by 4th October, 1957, on forms obtainable from, and returnable to, Group Secretary (L.86), 5, Collingham-gardens, London, S.W.5.

ST. PETER'S, ST. PAUL'S AND ST. PHILIP'S HOSPITALS. Required, REGISTRAR in Anæsthetics. Non-resident appointment on an annual basis.

Applications (12 copies), and names and addresses of 2 referees, to the House Governor, St. Peter's Hospital, Henrietta-street, London, W.C.2. Closing date 5th October, 1957.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy for a HOUSE PHYSICIAN (Senior House Officer) on 15th December, 1957.

Further particulars and form of application, which must be returned not later than 14th October, 1957, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

TOOTING BEC HOSPITAL, Tooting Bec-road, S.W.17. (Mental Hospital, over 2000 Beds.) Temporary JUNIOR HOSPITAL MEDICAL OFFICER (resident or non-resident) required to commence duty 30th September, 1957. The Hospital is within easy access of teaching centres in London. Offers good opportunities for study for higher qualifications.

Applications, with names of 2 referees, to be sent to the Physician-Superintendent within 2 weeks of the appearance of this advertisement.

UNIVERSITY COLLEGE HOSPITAL, Gower-street, W.C.1. (X-RAY DIAGNOSTIC DEPARTMENT.) Applications are invited for the following posts, vacant 1st October, 1957 :—

REGISTRAR in X-ray Diagnostic Department for 1 year in the first instance.

D.M.R. TRAINEE (graded Registrar or Senior House Officer according to experience). Trainees who have completed 1 year of the D.M.R. course will be considered for this appointment as well as those who have not yet started the course.

Preference will be given to applicants holding a higher medical or surgical qualification.

Applications, with names of 2 referees, to Administrator and Secretary by 28th September, 1957.

WESTMINSTER HOSPITAL, St. John's-gardens, S.W.1. Applications invited for post of REGISTRAR to Psychiatric Department for 1 year in first instance from 1st December, 1957. The Department is concerned with both adults and children and there are 12 Beds for adult inpatients.

Applications (4 copies), with names of 2 referees, to House Governor by 28th September.

WILLESDEN GENERAL HOSPITAL, Harlesden-road, London, N.W.10. Locum REGISTRAR ANÆSTHETIST required until the end of January, 1958.

Apply Hospital Secretary.

WIMBLEDON HOSPITAL, Thurstan-road, Copse Hill, S.W.20. RESIDENT HOUSE SURGEON (not pre-registration), vacant 1st October. Salary £577 10s.

Applications, giving age, qualifications, &c., and names and addresses of 2 referees, to the Secretary at above address.

ASCOT. HEATHERWOOD ORTHOPÆDIC HOSPITAL. (200 Beds.) Locum REGISTRAR (orthopædics) required throughout October.

Applications, giving full details of experience and names of 2 referees, to Secretary.

ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGEMENT COMMITTEE. E.N.T. SURGEON (Senior House Officer grade) required at Ashton-under-Lyne General Hospital. Vacant early October.

Applications, stating age, qualifications and experience with copies of 2 testimonials, to be forwarded to the Group Secretary, General Hospital, Ashton-under-Lyne, Lancs, as soon as possible.

BIRMINGHAM, 9. LITTLE BROMWICH GENERAL HOSPITAL. PÆDIATRIC HOUSE PHYSICIAN (Male or Female). Post vacant 23rd October, 1957. Recognised for D.C.H. Includes duties on infectious diseases ward, Neonatal Department and clinic.

Apply Physician-Superintendent.

BIRMINGHAM, 18. DUDLEY ROAD HOSPITAL. (780 Beds.) HOUSE SURGEON required in Obstetrics and Gynæcological Department (vacant 1st November, 1957). Recognised for pre-registration and M.R.C.O.G. The Department under the direction of a Senior Consultant Obstetrician, consists of 115 maternity beds, 100 neonatal cots, and 60 gynæcological beds.

Detailed applications, with copies of 3 recent testimonials, to the Group Secretary.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

(1) **Birmingham (Selly Oak) Group, Oak Tree-lane, Birmingham, 29**

REGISTRAR (pathology), Selly Oak and other hospitals (joint resident appointment with Senior House Officer). Now vacant. Wide experience in general pathology.

2) **Coventry No. 20 Group, Coventry and Warwickshire Hospital, Coventry**

REGISTRAR (anæsthetics), Coventry and Warwickshire and Gulson Hospitals. Experience specialty essential. Recognised F.F.A.R.C.S.

(3) **St. Margaret's Hospital Group 4, Great Barr-Park, Birmingham, 22a**

REGISTRAR (mental deficiency), Whole-time. Experience specialty/high qualification desirable. Hospital (1470 Beds) recognised for D.P.M. Resident/non-resident.

Application forms from Group Secretaries to be returned by 30th September, 1957.

BIRMINGHAM (SANATORIA) GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER at West Heath Hospital, Rednal-road, Birmingham, 31, now vacant. (207 Beds for the treatment of tuberculous and non-tuberculous chest cases.) The successful applicant will reside at the above Hospital (accommodation for single person only), and will be offered facilities for undertaking duties at the Birmingham Chest Clinic, Great Charles-street, Birmingham, 3.

Applications, stating age, qualifications, training and experience, together with copies of 3 recent testimonials, should be addressed to the Group Secretary, Birmingham (Sanatoria) Group Hospital Management Committee, Yardley Green Hospital, Birmingham, 9.

BIRMINGHAM. UNITED BIRMINGHAM HOSPITALS. THE BIRMINGHAM AND MIDLAND HOSPITAL FOR WOMEN, Showell Green-lane, SPARKHILL, BIRMINGHAM, 11. Applications are invited from registered medical practitioners for the post of RESIDENT GYNÆCOLOGICAL HOUSE SURGEON for duty with the Professorial Unit from the 1st December, 1957. The appointment is recognised for the M.R.C.O.G. and D.Obst. R.C.O.G.

Application forms obtainable from the House Governor at the above address, to be returned not later than 7th October, 1957.

BISHOP'S STORTFORD, HERTFORDSHIRE. HERTS AND ESSEX GENERAL HOSPITAL. (400 Beds.) Applications are invited for the post of HOUSE OFFICER (surgical), pre-registration. Salary £467 10s.–£522 10s. p.a., less £125 in respect of residential emoluments. Appointment to commence immediately. There is a pre-registration medical post for which the successful candidate will receive consideration at the termination of the surgical appointment.

Applications, stating age, nationality, qualifications, and experience, with copies of 2 recent testimonials or the names of referees, to the Hospital Secretary.

BARNSTAPLE. NORTH DEVON INFIRMARY. (105 Beds.) HOUSE SURGEON required ; recognised pre-registration appointment.

Applications to Group Secretary, 19, Alexandra-road, Barnstaple.

BATLEY, YORKSHIRE. THE GENERAL HOSPITAL. Applications are invited for the following resident posts :—

(*a*) SENIOR HOUSE OFFICER (orthopædic surgery and E.N.T.).

(*b*) HOUSE OFFICER (ophthalmology and general surgery).

Post recognised for D.O. (London and Edinburgh).

Married accommodation can be made available for the Senior post but it would not be suitable for children.

Applications for the Senior House Officer post would be considered on a Locum Tenens basis.

Applications with recent testimonials to be sent to the Administrative Officer, The General Hospital, Carlinghow Hill, Batley, as soon as possible.

BEDFORD GENERAL HOSPITAL, Bedford. (436 Beds.) NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. MEDICAL REGISTRAR, vacant mid-October ; appointment for 1 year, renewable for second year. Hospital may be visited by writing to Senior Physician.

Application forms obtainable from, and returnable to, Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BENENDEN CHEST HOSPITAL (Civil Service Sanatorium Society), BENENDEN, near CRANBROOK, KENT. (169 Beds.) SENIOR HOUSE OFFICER (resident) required, Male or Female, registered medical practitioner. Salary £715 p.a., plus untaxed free board and lodgings ; transferable superannuation scheme. The Hospital, which is independent of the National Health Service, is fully equipped for the treatment, including regular major thoracic surgery, of adult male and female patients with pulmonary disease, tuberculous and non-tuberculous.

Applications, stating age, qualifications, experience, with names of 2 referees, should be sent to the Chief Medical Officer as soon as possible.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 acute beds.) ORTHOPÆDIC HOUSE SURGEON (first, second or third post), vacant now. Offers good opportunity for general experience in busy acute general hospital. Approved pre-registration post. Fully qualified practitioners may apply. Recognised for F.R.C.S.

Apply Group Secretary.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. ASSISTANT PATHOLOGIST (Senior House Officer grade) required in Area Laboratory. Offers experience all branches of pathology.

Detailed applications to Group Secretary.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 Beds.) HOUSE PHYSICIAN (House Officer or Senior House Officer grading according to experience).

Apply Group Secretary.

BEXHILL HOSPITAL, Bexhill-on-Sea. (62 Beds.) HOUSE SURGEON (resident) required. Pre-registration post vacant now. National scale of salary.

Apply to Hospital Administrator.

BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (obstetrics and gynæcology) required for 1st November, 1957. Recognised for M.R.C.O.G. and D.Obst.R.C.O.G. (combined obstetrics and gynæcology). Based on Queen's Park Hospital, Blackburn (a general hospital with 83 obstetric/gynæcology beds), with duties at Royal Infirmary, Blackburn, and occasionally at Victoria Hospital, Accrington.

Applications, with names of 2 referees, to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BLACKBURN. ROYAL INFIRMARY. (262 general beds.) BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICERS or SENIOR HOUSE OFFICERS (casualty and orthopædics) (2) required 6th October and 26th October, 1957. Junior Hospital Medical Officer posts can be for any period up to 4 years. Recognised for F.R.C.S.

Apply to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BLACKBURN. ROYAL INFIRMARY. (262 general beds.) BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Locum JUNIOR HOSPITAL MEDICAL OFFICER or SENIOR HOUSE OFFICER (casualty and orthopædics) required 6th October, 1957.

Apply immediately to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BLACKPOOL. VICTORIA HOSPITAL. (354 Beds.) HOUSE SURGEON. Resident pre-registration post available on 1st October, 1957, in the Department of Surgery at this modern well-equipped Hospital with excellent facilities for gaining experience. Recognised for F.R.C.S.

Applications, stating age, experience and the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BOLTON. THE ROYAL INFIRMARY. (238 Beds.) BOLTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. RESIDENT SENIOR HOUSE OFFICER in Orthopædic Surgery. Tenable for 12 months and recognised for F.R.C.S.

Applications, stating age, nationality, qualifications, experience, and the names of 2 referees, should be sent immediately to Group Secretary, The Royal Infirmary, Bolton.

BOURNEMOUTH (near). CHRISTCHURCH HOSPITAL, HANTS. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT HOUSE SURGEON for General Surgery at the above Hospital of 334 Beds, which includes a new surgical unit of 56 Beds. The successful applicant will be required to attend surgical outpatient sessions at the Royal Victoria Hospital, Boscombe. The post, which is recognised for pre-registration purposes, becomes vacant on 1st October.

Applications to the Hospital Secretary.

BOURNEMOUTH (near). CHRISTCHURCH HOSPITAL, CHRISTCHURCH, HANTS. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of a RESIDENT SENIOR HOUSE OFFICER, (surgical) for the above Hospital of 334 Beds, including a new Surgical Unit of 56 Beds. The post becomes vacant on 1st September, 1957. There is no emergency surgery undertaken at the moment, but the successful applicant will attend surgical outpatient sessions at the Royal Victoria Hospital, Boscombe.

Applications to the Hospital Secretary, Christchurch Hospital.

BRIGHTON AND LEWES HOSPITAL MANAGEMENT COMMITTEE. NEW SUSSEX HOSPITAL FOR WOMEN AND SUSSEX MATERNITY HOSPITAL. OBSTETRIC AND GYNÆCOLOGICAL HOUSE SURGEON (Female). Obstetrics at Sussex Maternity (56 Beds) and Gynæcological Department (24 Beds) at New Sussex Hospital.

Applications, giving age, experience and names of 2 referees, to be sent to the Administrative Officer, New Sussex Hospital, Windlesham-road, as soon as possible.

BRIGHTON GENERAL HOSPITAL. BRIGHTON AND LEWES HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the position of HOUSE PHYSICIAN to the Geriatric Unit. This is a large Unit with an active rehabilitation section, which provides excellent clinical facilities. Vacant 1st November.

Applications, stating age, qualifications, and experience, together with copies of recent testimonials, should be sent to the Physician-Superintendent, Brighton General Hospital, Elmgrove, Brighton, 7.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (312 Beds.)

2 HOUSE PHYSICIANS end of September and October. Pre-registration.

2 HOUSE SURGEONS beginning and end of October. Pre-registration and recognised for F.R.C.S.

Applications, stating usual particulars, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BURTON-ON-TRENT. THE GENERAL HOSPITAL. HOUSE SURGEON (general and pre-registration) required immediately at the above Hospital. Post recognised for F.R.C.S.

Applications to Group Secretary as soon as possible.

BRISTOL. COSSHAM AND FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER required for the Department of Thoracic Surgery (120 Beds) at Frenchay Hospital.

Apply to Group Secretary, Frenchay Hospital, Bristol, giving age and experience and quoting 2 referees.

BROXBURN, WEST LOTHIAN. BANGOUR GENERAL HOSPITAL, near EDINBURGH. MAXILLO-FACIAL AND PLASTIC SURGERY UNIT. Locum HOUSE OFFICER (pre-registration post) required in the Maxillo-Facial and Plastic Surgery Unit of Bangour General Hospital, Broxburn.

Applications to the Group Secretary and Treasurer, Board of Management, Bangour Hospital, Broxburn, West Lothian.

CAERPHILLY HOSPITAL. (226 Beds for acute general medicine and surgery.) Pre-registration HOUSE OFFICER (orthopædics and general surgery) required at above Hospital.

Apply immediately, with names of referees, to the Group Secretary, Rhymney and Sirhowy Valleys Hospital Management Committee, Central Offices, Caerphilly-road, Ystrad Mynach, Glam.

CAMBRIDGE. THE UNITED CAMBRIDGE HOSPITALS. REGISTRAR in Infectious Diseases (residence available), Brookfields Hospital, Cambridge, which is the Poliomyelitis Centre for the South-West section of East Anglia and the Infectious Diseases Hospital of the United Cambridge Hospitals. There is also a ward for tuberculosis, and 1 for general medicine. Appointment for 1 year in first instance, renewable for a second year. Vacant from mid-October.

Apply, with full particulars and names of 3 referees, to Secretary, Addenbrooke's Hospital by 2nd October.

CHELMSFORD. ST. JOHN'S HOSPITAL. Applications are invited from registered practitioners for the post of RESIDENT PÆDIATRIC HOUSE OFFICER (Male or Female), commencing 8th October, 1957, to work in the Pædiatric Unit of the Chelmsford Hospital Group. The unit includes a premature baby nursery of 10 Cots and a neonatal department in the maternity block of the Hospital. The Department is recognised for the D.C.H.

Applications, stating age, nationality, qualifications and experience, together with recent testimonials, should be received not later than 24th September, by the Group Secretary, Chelmsford Group Hospital Management Committee, Chelmsford and Essex Hospital, London-road, Chelmsford.

CHICHESTER. ROYAL WEST SUSSEX HOSPITAL. (202 acute beds.) RESIDENT HOUSE SURGEON required for 6 months appointment. National salary scale for either provisionally or fully registered practitioners. Post approved for pre-registration practitioners and F.R.C.S. 7 Residents including Resident Surgical Officer and 3 House Surgeons. Vacant 13th October.

Applications, stating age, experience, qualifications, with references or names of referees, to Senior Administrative Officer.

CHICHESTER. ROYAL WEST SUSSEX HOSPITAL. (202 acute beds.) RESIDENT HOUSE PHYSICIAN required for 6 months appointment. National salary scale for either provisionally or fully registered practitioners. Post approved for pre-registration practitioners. 7 residents, including Resident Medical Officer and House Physician. Vacant 15th October, 1957.

Applications, stating age, qualifications, with references or names of referees, to Senior Administrative Officer.

CUCKFIELD HOSPITAL, Cuckfield, near Haywards HEATH, SUSSEX. JUNIOR HOUSE SURGEON (resident), Orthopædic and Traumatic Unit. Pre-registration recognition applied for. Post now vacant. Tenable 6 months.

Applications, giving age, nationality, qualifications and experience, with names of 2 referees, to Group Secretary, Mid-Sussex Hospital Management Committee.

CARLISLE. CUMBERLAND INFIRMARY. Locum HOUSE OFFICER required. Gynæcology with some obstetrics. Period of 3 months from 1st November, 1957.

Apply to the Group Secretary, East Cumberland Hospital Management Committee, Cumberland Infirmary, Carlisle.

CARDIFF (near). PRINCE OF WALES ORTHOPÆDIC HOSPITAL, RHYDLAFAR, near CARDIFF. SENIOR HOUSE OFFICER required. Regional Orthopædic Centre for South Wales area. 281 Beds and branch hospital of 70 Beds. Outpatient clinic in Cardiff. Full staff of Consultants and Registrars. Single accommodation available at Hospital at Rhydlafar.

Form of application from Group Secretary, 44, Cathedral-road, Cardiff.

CARDIFF. THE UNITED CARDIFF HOSPITALS. Applications are invited for the post of SENIOR HOUSE OFFICER (medical) to the Miners' Chest Diseases Treatment Centre at Llandough Hospital, Penarth. The Centre caters for all types of chest diseases and it is closely associated with the adjoining Pneumoconiosis Research Unit of the Medical Research Council.

Application forms are available from the Secretary to the Board at the Cardiff Royal Infirmary, Newport-road, Cardiff, and should be returned within 14 days of the appearance of this advertisement.

CARDIFF. THE UNITED CARDIFF HOSPITALS. Applications are invited for the appointment of SENIOR REGISTRAR to the Department of Physical Medicine at the Cardiff Royal Infirmary to commence 1st December.

Application forms are available from the Secretary to the Board at the Cardiff Royal Infirmary, Newport-road, Cardiff, and should be returned not later than 14 days after the appearance of this advertisement.

CARDIFF. ST. DAVID'S HOSPITAL. Resident Obstetrical HOUSE OFFICER (recognised for M.R.C.O.G.) required in Maternity Department at above Hospital, commencing 1st November, 1957.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

CARDIFF. ST. DAVID'S HOSPITAL. Senior House OFFICER required for Accident Unit at above Hospital.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

CARSHALTON, SURREY. QUEEN MARY'S HOSPITAL FOR CHILDREN. (A general children's hospital of 700 Beds.) HOUSE SURGEON (House Officer) (resident) required for 6 months (3 months general surgery, 3 months E.N.T. and orthopædics). Applicants must have completed 12 months Pre-registration Service.

Applications, stating age and qualifications, together with 1 recent testimonial and the names of 2 referees, should be submitted to the Group Secretary, immediately.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for :—

Essex County Hospital, Colchester, Essex (185 Beds)

Post of SENIOR HOUSE OFFICER to Casualty and E.N.T. Departments.

Post of SENIOR HOUSE OFFICER to Casualty and Radiotherapy Departments.

Posts tenable for 6 months or 1 year. Recognised for F.R.C.S.

Black Notley Hospital, Braintree, Essex (516 Beds)

Post of HOUSE OFFICER (orthopædic surgery). Duties include care of cases from London Hospital Orthopædic Department. First, second, third, or pre-registration post, tenable for 6 months. Recognised for F.R.C.S.

Post of Locum ORTHOPÆDIC REGISTRAR with some duties at the London Hospital required immediately to 6th October.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

DERBY. DERBYSHIRE ROYAL INFIRMARY. (416 Beds.) SENIOR HOUSE OFFICER (casualty), vacant 2nd November. Recognised for periods of 6 months casualty training for F.R.C.S. The staffing of the department is a Senior Casualty Officer and 2 Senior House Officers.

Apply, stating age, experience, and 2 names for reference, to Secretary.

DRIFFIELD, YORKSHIRE. EAST RIDING GENERAL HOSPITAL. (247 Beds.) HOUSE PHYSICIAN, approved pre-registration post. Fully qualified practitioners may apply. Duties include acute and chronic medicine. Good general experience for first house appointment.

Apply Group Secretary, Westwood Hospital, Beverley, Yorkshire.

EAST ANGLIAN REGIONAL HOSPITAL BOARD.

MEDICAL REGISTRAR, Peterborough Hospital Group. Principal hospital, Peterborough Memorial—150 Beds. Duties may include work in Isolation Hospital, St. John's Hospital and Thorpe Hall Annexe. Appointment for 1 year, renewable for second year.

ANÆSTHETIC REGISTRAR, Peterborough Memorial Hospital and Annexes. Post recognised for D.A. and F.F.A.R.C.S. and provides experience in all departments including a Thoracic Unit. Appointment for 1 year, renewable for second year.

Applications, stating age, experience and the names of 3 referees, to the Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 30th September, 1957. Candidates invited to visit the hospitals by direct arrangement with Hospital Management Committee Secretary, Memorial Hospital, Peterborough.

EDINBURGH. CHALMERS HOSPITAL. Applications are invited from registered or pre-registration medical practitioners for appointment of RESIDENT HOUSE SURGEON in the Gynæcological Annexe of the above Hospital, for 6 months commencing 1st October, 1957, entailing responsibility for 24 gynæcological beds and 19 children's surgical beds.

Applications, stating age, qualifications and experience, and names of 2 referees, to be sent immediately to the Secretary, Edinburgh Central Hospitals, 1, Rillbank-terrace, Edinburgh.

EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom, SURREY. RESIDENT ANÆSTHETIST (Senior House Officer grade) required. 12 months appointment recognised for F.F.A.R.C.S.

Applications, stating age, qualifications and experience, with copies of 2 recent testimonials, should be sent as soon as possible to Group Secretary at above address.

EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom, SURREY. RESIDENT HOUSE PHYSICIAN required 1st November. Fully registered post.

Applications, stating age, qualifications and experience, with copies of 2 recent testimonials, should be sent as soon as possible to Group Secretary at above address.

GLASGOW NORTHERN HOSPITALS BOARD OF MANAGEMENT. Applications are invited for 2 immediate vacancies for JUNIOR HOSPITAL MEDICAL OFFICERS in the Infectious Diseases Department (450 Beds). Excellent experience in infectious diseases and general medicine. Undergraduate and postgraduate teaching unit and Regional centre for treatment of poliomyelitis.

Applications, stating age, nationality, qualifications, and experience with names of 2 referees, to Physician-Superintendent, Ruchill Hospital, Glasgow, N.W.

GLASGOW NORTHERN HOSPITALS BOARD OF MANAGEMENT. Applications are invited for 2 immediate vacancies for JUNIOR HOSPITAL MEDICAL OFFICERS, Ruchill Hospital, Glasgow, N.W., in the Chest Department (Medical Unit). The department consists of 200 Beds for the treatment of pulmonary tuberculosis and other diseases of the chest. There is attached to the department a Thoracic Surgical Unit of 60 Beds. Facilities are available for postgraduate study and research.

Applications, stating age, nationality, qualifications, and experience, with names of 2 referees, to Physician-Superintendent immediately.

GLASGOW. VICTORIA INFIRMARY. Applications are invited for the post of SENIOR HOUSE OFFICER in Orthopædics for duties at the Victoria Infirmary, Glasgow, and a large unit at the Victoria Auxiliary Infirmary, Philipshill. The post, which is tenable for 1 year, is resident at Philipshill.

Applications, with names of 2 referees, to the Secretary, Board of Management for Glasgow Victoria Hospitals, 24, St. Vincent-place, Glasgow, C.1.

GLOUCESTERSHIRE ROYAL HOSPITAL, Southgate-street, GLOUCESTER. RESIDENT ANÆSTHETIST required, Senior House Officer grade. Post recognised for the F.F.A. R.C.S., and vacant 1st October.

Applications, naming 2 referees, to Group Secretary.

GRIMSBY GENERAL HOSPITAL. Applications are invited for the post of HOUSE SURGEON (gynæcology), pre-registration or Senior House Officer grade, with some relief obstetric duties. Post vacant 15th October, 1957. Senior House Officer post recognised for M.R.C.O.G. Up-to-date Medical Library and reading facilities available.

Apply, with 2 names for reference, to Hospital Secretary, Grimsby General Hospital, Grimsby.

GUILDFORD. ROYAL SURREY COUNTY HOSPITAL. (233 Beds.) CASUALTY OFFICER required. The post is recognised for F.R.C.S. examination and the grading is that of Senior House Officer. 2 Casualty Officers are employed who share the work of the department which is part of the orthopædic and traumatic unit. Regular instruction is given in traumatic surgery and the Casualty Officers take part in the work of the fracture clinics. Post is vacant late October.

Applications, with copies of testimonials, to the Hospital Secretary.

HARROGATE AND DISTRICT GENERAL HOSPITAL. (253 Beds. Recognised for D.Obst.R.C.O.G.) Applications are invited for the resident post of SENIOR HOUSE OFFICER in Obstetrics and Gynæcology, vacant 1st November, 1957.

Applications, naming 2 referees, should reach the Hospital Secretary, Harrogate and District General Hospital, Harrogate, Yorkshire, as soon as possible.

HERTFORD COUNTY HOSPITAL. (173 Beds. Hospital situated 21 miles from London.) RESIDENT CASUALTY OFFICER (Senior House Officer grade) with attachment to Pædiatrician and Ophthalmic Consultant. Salary £819 10s. p.a., less £150 p.a. residential emoluments. Recognised under F.R.C.S. regulations. Appointment to commence as soon as possible.

Apply, with full details and references, to Group Secretary, Hertford Hospital Management Committee, County Hospital, Hertford, Herts.

HITCHIN, HERTFORDSHIRE. LISTER HOSPITAL. RESIDENT HOUSE SURGEON required. Post vacant 2nd October, 1957. Recognised as pre-registration post and for F.R.C.S.

Applications, stating age, nationality, qualifications, and experience, together with copies of 3 recent testimonials, to be sent to the Medical Administrator.

HITCHIN. LISTER HOSPITAL. (330 Beds.) North West METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time MEDICAL REGISTRAR (resident) required at above Hospital. Post gives good all-round experience in general medicine and pædiatrics, valuable for the M.R.C.P. Vacant 7th November, 1957. Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, Secretary, Luton and Hitchin Group Hospital Management Committee, St. Mary's Hospital, Luton, Beds, by 7th October, 1957.

HITCHIN. NORTH HERTS HOSPITAL. Applications are invited for the post of RESIDENT HOUSE SURGEON, vacant 22nd September, 1957. Recognised for the F.R.C.S.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to be sent to the Medical Administrator, Lister Hospital, Hitchin, as soon as possible.

HITCHIN, HERTFORDSHIRE. NORTH HERTS HOS-PITAL. RESIDENT HOUSE SURGEON in Obstetrics and Gynæcology required for 6 months from mid-October. Duties include the maternity wards (42 Beds) and gynæcological ward (20 Beds). The post is recognised for the D.Obst.R.C.O.G.

Applications, stating age, qualifications and experience, together with copies of 3 recent testimonials, to be sent to the Medical Administrator, Lister Hospital, Hitchin, as soon as possible.

HOVE GENERAL HOSPITAL, Sussex. (75 Beds. 3 Resident Medical Officers.) Pre-registration HOUSE PHYSICIAN required at the beginning of October, 1957. Excellent clinical material available. Post is suitable for candidate working for higher degree. Salary £425–£525, less £125 p.a. for residential emoluments.

Applications, stating age, qualifications, full details of experience, together with the names and addresses of 2 referees, to the Administrative Officer.

HOVE GENERAL HOSPITAL, Sussex. (75 Beds. 3 Resi-dent Medical Officers.) Pre-registration HOUSE SURGEON (with casualty duties) required from 24th September, 1957, for 6 months. This post, which is recognised for F.R.C.S., provides a wide experience in an active surgical unit. Salary £467 10s.–£577 10s., less £125 p.a., for residential emoluments.

Applications, stating age, qualifications, full details of experience, together with names and addresses of 2 referees, to the Administrative Officer.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required to commence duty immediately. The post is recognised as a pre-registration appointment and for the F.R.C.S. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Secretary to the Management Committee.
The Royal Infirmary, Huddersfield.

HEMEL HEMPSTEAD. WEST HERTS HOSPITAL. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. ANÆSTHETIC REGISTRAR required at above Hospital. New post. Application made for recognition by Faculty.

Application forms obtainable from, and returnable to, Secretary, West Herts Group Hospital Management Committee, 9, Rickmansworth-road, Watford, Herts, by not later than 10 days after the appearance of this advertisement.

HULL. VICTORIA HOSPITAL FOR SICK CHILDREN, Park-street. Pre-registration or registered post. HOUSE SURGEON required 21st October. Recognised for D.C.H. An interesting and varied post which includes outpatient and casualty work.

Applications, together with details of experience, testimonials, to the Hospital Secretary.

ILKLEY. MIDDLETON HOSPITAL. (430 Beds.) RESIDENT JUNIOR HOSPITAL MEDICAL OFFICER required at the above Hospital. This appointment provides for experience in the specialties of tuberculosis and geriatrics.

Applications, stating age, nationality, qualifications and experience, to Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL. Anglesea ROAD WING. (356 Beds.) Applications are invited for the post of SENIOR HOUSE SURGEON to the Fracture and Orthopædic Department. The post is graded Senior House Officer and is recognised for the F.R.C.S. examinations. The Department has 2 Consultants, about 60 Beds and a large outpatient attendance ; it offers wide experience.

Applications, stating age, nationality and experience, together with copies of recent testimonials, to the Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL. Anglesea ROAD WING. (356 Beds.) Applications are invited for the post of HOUSE SURGEON to the E.N.T. and Ophthalmic Departments. The post is recognised for pre-registration and for the D.L.O. examination.

Applications, giving full particulars and copies of recent testimonials, to Hospital Secretary.

IPSWICH. ST. HELEN'S HOSPITAL. (129 Beds for infectious diseases, pulmonary tuberculosis, long-stay orthopædics and geriatrics. The area Chest Clinic is in the Hospital.) HOUSE PHYSICIAN required (post-registration appointment). Accommodation available for married man.

Applications to JOHN WILLIAMS, Group Secretary, Ipswich Group Hospital Management Committee, at the Ipswich and East Suffolk Hospital (Anglesea Road Wing), Ipswich.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston UPON THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of Locum SENIOR HOUSE OFFICER (orthopædic and casualty) from 1st October, 1957, for approximately 4 weeks.

Applications, stating age, qualifications and experience with 2 recent testimonials, should reach the Physician-Superintendent of the Hospital as soon as possible.

LANARK. BELLEFIELD SANATORIUM. Resident JUNIOR HOSPITAL MEDICAL OFFICER required for above Sanatorium.

Applications to the Secretary, Board of Management for Glasgow Victoria Hospitals, 24, St. Vincent-place, Glasgow, C.1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. Applications are invited for a post of REGISTRAR in Pathology for duties initially at The Women's Hospital to take up duty as soon as possible for the period to 30th September, 1958. Annual reappointment thereafter until completion of the normal period of training will be considered without need for further application.

Apply by 12th October, 1957, on form obtainable from the Secretary, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. THE WOMEN'S HOSPITAL. Applications are invited for a post of SENIOR HOUSE OFFICER in Gynæcology (resident) to take up duty as soon as possible for the period to 30th September, 1958.

Apply by 10th October on form obtainable from the Secretary, 80, Rodney-street, Liverpool, 1.

LEEDS REGIONAL HOSPITAL BOARD. Registrar vacancies.

Anæsthetics

(i) Halifax Group (approximately 340 Beds in the surgical specialties). Resident.

(ii) Hull A, Hull B and East Riding Groups. Recognised for the F.F.A.R.C.S. Duties may include thoracic anæsthesia. Non-resident. Vacant October.

General Medicine

(i) Hull A Group (294 general medical beds) and East Riding Group (78 general medical beds). Duties 6/11 Hull A and 5/11 East Riding. Holder to reside in Beverley.

(ii) Halifax Group (110 general medical beds) (380 geriatric beds). Duties divided equally between general medicine and geriatrics. Non-resident.

Orthopædic Surgery

Harrogate General Hospital (38 orthopædic beds). Non-resident.

Plastic Surgery

St. James's Hospital, Leeds. Non-resident. Special plastic and maxillo-facial unit. (72 Beds.)

Psychiatry

(i) Menston Hospital, near Leeds (2500 Beds).

(ii) Oulton Hall Hospital, near Wakefield (272 Beds), and affiliated mental deficiency colonies. Non-resident.

(iii) Stanley Royd Hospital, Wakefield (2000 Beds).

If desired facilities for attendance at the Leeds University will be provided if the successful candidates are studying for the D.P.M.

Applications, stating age, qualifications and details of present and previous appointments with dates, together with the names and addresses of 3 referees, to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 28th September, 1957.

LEEK (near). ST. EDWARD'S HOSPITAL, Cheddleton, near LEEK, STAFFORDSHIRE. JUNIOR HOSPITAL MEDICAL OFFICER. Previous mental hospital experience not essential. This hospital offers opportunities for gaining experience in all branches of psychiatry. Terms and conditions of service will be as approved for hospital medical staff employed in the National Health Service. Salary £852–£55–£1182. Single furnished quarters, or unfurnished house on hospital estate available for a married man.

Applications as soon as possible to "The Medical Superintendent."

LUTON AND DUNSTABLE HOSPITAL, Luton, Bedfordshire. Locum SURGICAL REGISTRAR (resident) required for 4 weeks from 30th September to 27th October, 1957.

Applications, giving full particulars and names of referees, to Secretary, Luton and Dunstable Hospital, Luton, Beds.

MANCHESTER, 4. ANCOATS HOSPITAL. Applications are invited for the post of CASUALTY OFFICER (Senior House Officer). Recognised for F.R.C.S. Vacant 19th November, 1957.

Applications, with names of 2 referees, by 30th September, 1957, to Group Secretary, North Manchester Hospital Management Committee, Crumpsall Hospital, Manchester, 8.

MANCHESTER. BOOTH HALL CHILDREN'S HOSPITAL, BLACKLEY, MANCHESTER, 9. (380 Beds. Recognised for D.C.H.)

RESIDENT SENIOR HOUSE OFFICER (surgical).

Applications, giving names and addresses of 2 referees, to be sent to Group Secretary, from whom further particulars may be obtained.

HOUSE OFFICER (surgical), pre- or post-registration. Duties mainly general surgery and neurosurgery. Post vacant 8th October.

Applications, with usual particulars and copies of 2 recent testimonials, to Group Secretary.

MANCHESTER REGIONAL HOSPITAL BOARD. Bolton DISTRICT GENERAL HOSPITAL. (607 Beds, including 107 for obstetrics and 30 for gynæcology). REGISTRAR in Obstetrics and Gynæcology. Hospital recognised for M.R.C.O.G. and D.Obst.R.C.O.G.

Applications, stating age, nationality, qualifications, experience, and the names of 2 referees, should be sent to Group Secretary, Bolton and District Hospital Management Committee, The Royal Infirmary, Bolton, not later than 24th September, 1957.

MANCHESTER REGIONAL HOSPITAL BOARD. REGISTRAR in Pathology to the Bolton and District Group of hospitals with main duties in the Group Laboratories at the Bolton Royal Infirmary and the Bolton District General Hospital. Recognised for the Dip.Path.

Applications, with the names of 2 referees, should be sent immediately to Group Secretary, Bolton and District Hospital Management Committee, The Royal Infirmary, Bolton.

MANCHESTER, 19. THE DUCHESS OF YORK HOSPITAL FOR BABIES. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. There is an immediate vacancy at the above Hospital, which is associated with the Manchester University for teaching purposes, for a RESIDENT HOUSE OFFICER (Male or Female) post or second pre-registration, for 6 months.

Applications, with copies of 3 testimonials, to be sent immediately to the Administrative Officer at the above address.

MANCHESTER, 20. CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER (radiotherapy) at the above Hospital. Training will be available from October, 1958, for Diploma in Radiotherapy course.

Applications, with full details and the names of 2 referees, to the Group Secretary, Withington Hospital, Manchester, 20, immediately.

MANCHESTER, 23. WYTHENSHAWE HOSPITAL SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (E.N.T.) at the above-mentioned Hospital, with some duties at other hospitals in the Group. This post is recognised by the Royal College of Surgeons of England as a Senior House Officer (E.N.T.) post.

Applications, stating age, qualifications, present post, experience and names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, within 7 days of the appearance of this advertisement.

NORTHWOOD, MIDDLESEX. MOUNT VERNON HOSPITAL. (551 Beds.) NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required in the X-ray Diagnostic Department at above Hospital for 1 year in first instance.

Application forms obtainable from, and returnable to, the Group Secretary, Harefield and Northwood Group Hospital Management Committee, Mount Vernon Hospital, Northwood, Middlesex, by 5th October, 1957. Hospital may be visited by direct appointment.

NORWICH. NORFOLK AND NORWICH HOSPITAL. Locum ORTHOPÆDIC REGISTRAR required for period 14th October–23rd December, 1957. Resident or non-resident. Salary £19 5s. per week in accordance with terms and conditions of service of hospital medical staff. Membership of a Medical Defence Society is a condition of appointment.

Applications, stating age, qualifications and experience, together with names of 2 referees, to Group Secretary, Hospital Management Committee, St. Stephen's-road, Norwich.

NOTTINGHAM. CITY HOSPITAL. (811 Beds.) Applications are invited for the post of RESIDENT PATHOLOGIST (Senior House Officer). Previous experience an advantage. Post vacant 14th November, 1957.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 testimonials, to be sent to the Group Secretary, Sherwood Hospital, Hucknall-road, Nottingham.

NOTTINGHAM. CITY HOSPITAL. (811 Beds.) Applications are invited for the post of HOUSE SURGEON, vacant 4th November, 1957. Recognised for pre-registration purposes.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. A Senior HOUSE OFFICER (orthopædic and fracture) required 30th September. Post offers exceptional experience in traumatic surgery.

Applications, stating age, qualifications, experience, nationality together with copies of testimonials, to be sent to Group Secretary.

NOTTINGHAM GENERAL HOSPITAL. E.N.T. Department. A SENIOR HOUSE OFFICER (E.N.T.) required at above Hospital. This post is recognised for the D.L.O. and F.R.C.S. examinations. Salary and conditions of service in accordance with Ministry regulations. Duties to commence about end September.

Applications, stating age, qualifications, experience and nationality, together with copies of testimonials, to be sent to Group Secretary.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the whole-time non-resident appointment of REGISTRAR in the Department of Psychological Medicine at the Royal Victoria Infirmary. Facilities are given to take the Durham D.P.M. course and duties varied to provide all types of inpatient and outpatient experience, including child psychiatry. The appointment is for 1 year in the first instance and will be subject to Ministry of Health terms and conditions of service for hospital medical staff in the National Health Service.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.
Royal Victoria Infirmary, Newcastle upon Tyne.

NORTHAMPTON GENERAL HOSPITAL. (482 Beds.) Vacancies 1st October, 1957, for the following :—

HOUSE OFFICER (Fracture and Orthopædic Department). Recognised for F.R.C.S. and for pre-registration.

SENIOR HOUSE OFFICER (general surgery), with some duties at Northampton General Hospital but mostly for General Surgical Unit at Manfield Orthopædic Hospital.

6 months appointments in first instance.

Applications as soon as possible to S. G. HILL, Superintendent.

NORTHAMPTON. MANFIELD ORTHOPÆDIC HOSPITAL. (200 Beds.) Vacancy 1st October, 1957, for SENIOR HOUSE OFFICER. The post provides good experience at orthopædic outpatient clinics and is recognised for F.R.C.S. 6 months appointment in first instance.

Applications, as soon as possible, to S. G. HILL.
General Hospital, Northampton.

OXFORD. NUFFIELD ORTHOPÆDIC CENTRE, Headington, OXFORD. Applications are invited from suitably qualified persons for a SENIOR HOUSE OFFICER grade appointment, vacant 14th October, and another on 1st November, 1957.

Applications, with names of referees, to be sent to the Secretary as soon as possible.

PETERBOROUGH. THE MEMORIAL HOSPITAL. PETERBOROUGH AND STAMFORD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON.

Applications, with testimonials, should be addressed to the Secretary, Memorial Hospital, Peterborough.

PLYMOUTH. MOUNT GOLD HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER for the Orthopædic and Fracture Service, centring on Mount Gold Hospital and associated hospitals. Post recognised by R.C.S. Vacancy commencing from 1st October, 1957.

Applications, stating age, qualifications, with dates, &c., and with copies of 2 recent testimonials, to be forwarded to the Secretary, Mount Gold Hospital, Plymouth, within 14 days of this advertisement appearing.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE. INFECTIOUS DISEASES HOSPITAL. SENIOR HOUSE OFFICER required with duties also on the Tuberculosis Wards and the Poliomyelitis Diagnostic and Respiratory Centre. Vacant 1st October, 1957.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be forwarded as soon as possible to E. H. HURST.

St. Mary's Hospital, Milton-road, Portsmouth.

ROMFORD GROUP HOSPITAL MANAGEMENT COMMITTEE. CLINICAL ASSISTANT required on the staff of the Regional Ophthalmic Centre at Oldchurch Hospital, Romford, to undertake 1 outpatient session per week (Thursday morning) in the Eye Clinic at Tilbury and Riverside Hospital, Tilbury.

Applications to be sent to Group Secretary, Oldchurch Hospital, Romford, as soon as possible.

ROMFORD, ESSEX. VICTORIA HOSPITAL. (99 Beds.) RESIDENT HOUSE PHYSICIAN (Male) required from 1st October, 1957. Not pre-registration appointment.

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) RESIDENT SENIOR HOUSE OFFICER in Anæsthetics. Post recognised for F.F.A.R.C.S. Excellent opportunities exist at this Hospital for gaining tuition and experience in the administration of anæsthetics. The equipment is the most modern available.

Applications should be sent to Group Secretary, Romford Hospital Management Committee, at the Hospital as soon as possible.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) SENIOR HOUSE OFFICER (ophthalmology).

Applications should be addressed immediately to the Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROCHDALE INFIRMARY. Rochdale and District Hospital MANAGEMENT COMMITTEE. HOUSE SURGEON (resident) required. Pre- or post-registration Doctors eligible for this post, which is recognised for 6 months F.R.C.S. experience.

Apply at once to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale.

ROCHDALE AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. BIRCH HILL HOSPITAL. HOUSE OFFICER (obstetrics and gynæcology) required early November. Pre- or post-registration post of 6 months duration. Recognised for D.Obst.R.C.O.G.

Apply to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, at once.

READING AREA HOSPITALS. Applications are invited for the post of SENIOR HOUSE OFFICER (pathology). Post vacant 15th October, 1957. Previous experience in pathology desirable, but not essential. Salary £819 10s. (less £150 board residence).

Apply, stating age, qualifications with dates, nationality, present post, together with the names of 3 referees, to Group Secretary, 3, Craven-road, Reading.

READING. BATTLE HOSPITAL. (391 Beds.) Applications are invited from registered medical practitioners for the post of RESIDENT JUNIOR HOUSE SURGEON in the Accident and Orthopædic Department. Post vacant 1st November, 1957. F.R.C.S. recognised. Also casualty duties.

Apply, stating age, qualifications with dates, nationality, present post, with 1 copy of recent testimonial, to Hospital Secretary.

READING COMBINED HOSPITALS. Area Department OF OBSTETRICS AND GYNÆCOLOGY. (100 Beds.) Applications are invited from registered medical practitioners, Male and Female, for the resident appointment of GYNÆCOLOGICAL HOUSE SURGEON at the Royal Berkshire Hospital, Reading. Vacant 8th October, 1957, and tenable for 6 months. Post recognised for M.R.C.O.G.

Write, stating age and qualifications with dates, nationality and present post, with copy of 1 recent testimonial, to Secretary.

SALISBURY GENERAL HOSPITAL. Locum Resident HOUSE SURGEON required from 2nd November to 30th November, 1957.

Apply as soon as possible, giving the names and addresses of 2 referees, to Group Secretary, Salisbury Group Hospital Management Committee, Odstock Hospital, Salisbury.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance.

SENIOR REGISTRAR in Radiotherapy based at the Western Infirmary, Glasgow.

REGISTRAR in Surgery based at the Royal Alexandra Infirmary, Paisley.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 5th October, 1957.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. REGISTRAR in Medicine, Royal Infirmary of Edinburgh.

Apply, giving particulars of age, qualifications and previous experience, and the names of 2 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, by 12th October.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. SENIOR REGISTRAR in Ophthalmology to the Professorial Unit at the Royal Infirmary of Edinburgh.

Apply, giving particulars of age, qualifications and previous experience, and the names of 3 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, by 12th October.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS BOARD OF GOVERNORS AND SHEFFIELD REGIONAL HOSPITAL BOARD. Reciprocal Training Scheme for Senior Registrars. Whole-time NON-RESIDENT SENIOR MEDICAL REGISTRAR required with initial tenure of appointment at the City General Hospital, Sheffield. The Hospital has teaching affiliations with Sheffield University and most of the Consultant staff have the status of Clinical Teachers. There is a Professorial Medical Unit and a Regional Cardiological Department. Appointment for 1 year in first instance and renewable thereafter annually. The successful candidate will be transferred to the Teaching Hospitals for the second phase of the appointment in accordance with arrangements under the Reciprocal Training Scheme. Renewal of appointment and transfer to the Teaching Hospitals will be subject to satisfactory work and progress.

Further details and form of application from the Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, 10. Forms to be returned by 7th October, 1957.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications invited for the post of SENIOR REGISTRAR in Clinical Pathology. Possession of a higher qualification desirable but not essential. The appointment is for 1 year in the first instance and will be reviewed annually. It has been agreed in principle between the Board of Governors of The United Sheffield Hospitals and the Sheffield Regional Hospital Board that the appointment, if extended for the full period, will be divided, subject to the satisfactory work and progress, between The United Sheffield Hospitals and a hospital in the Region (at present the Derbyshire Royal Infirmary).

Applications, stating age, qualifications, and experience, with the names of 3 referees, should be sent not later than 25th September, 1957, to the Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield 1.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications invited for the post of REGISTRAR in Clinical Pathology. The successful candidate may be required to work in any of the laboratories of the United Sheffield Hospitals.

Applications, stating age, qualifications, and experience, with the names of 3 referees, should be sent not later than 25th September, 1957, to the Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. CHILDREN'S HOSPITAL. Applications are invited from registered medical practitioners for the resident post of HOUSE PHYSICIAN to the Professorial Unit at the above Hospital. Vacant 1st November, 1957.

Applications, stating age, qualifications, and experience, with the names of 3 referees or copy testimonials, should reach the Superintendent, Children's Hospital, Western Bank, Sheffield, 10, not later than 30th September, 1957.

SHEFFIELD. CITY GENERAL HOSPITAL. (652 Beds. Recognised for training for F.R.C.S. examination.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT REGISTRAR (casualty and orthopædic duties) required immediately. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 30th September, 1957, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD. CITY GENERAL HOSPITAL. (652 Beds. Recognised for Final Fellowship examination.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (thoracic surgery) required. Appointment for 1 year in first instance. General Hospital with Regional Department of Cardiology. Thoracic Surgical Unit deals with tuberculosis and non-tuberculosis cases. Previous thoracic surgical experience desirable.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 30th September, 1957, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD NATIONAL CENTRE FOR RADIOTHERAPY. SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT SENIOR HOUSE OFFICER or REGISTRAR in Radiotherapy required. (Possession of a higher qualification in Medicine or Surgery or the D.M.R.(T.) Part I, would qualify for appointment of Registrar.) Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 30th September, 1957, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD. NETHER EDGE HOSPITAL. Applications are invited for the resident post of SENIOR HOUSE OFFICER. Main duties will be in connection with the Maternity Unit and also in the wards for long-stay medical cases. The post is not recognised for the D.Obst.R.C.O.G. Small flat available on rental.

Apply, giving full details of age, qualifications, present and previous appointments with dates, and the names of 2 persons for reference, to the Group Secretary, Nether Edge Hospital, Sheffield, 11.

SHREWSBURY. EYE, EAR AND THROAT HOSPITAL. SENIOR HOUSE OFFICER (E.N.T.) Duties at E.N.T. Hospital (68 Beds) and Copthorne Hospital (168 Beds). Post recognised for the D.L.O.R.C.S. Vacant 1st November, 1957.

Applications, with copy testimonials, to the Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY AND COPTHORNE HOSPITAL. (500 Beds.) RESIDENT ANÆSTHETIST (Senior House Officer). Post recognised for F.F.A.R.C.S. Registrar also employed. Vacant mid-September.

Applications and copy testimonials to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY/COPTHORNE HOSPITAL. (500 Beds.) HOUSE PHYSICIAN, pre-registration candidates eligible. Vacant 24th October, 1957.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY/COPTHORNE HOSPITAL. (500 Beds.) SHREWSBURY HOSPITAL GROUP. HOUSE SURGEON, vacant 1st November, 1957. Pre-registration candidates eligible. Recognised for the F.R.C.S.

Applications, with copy testimonials, to Group Secretary, Royal Salop Infirmary, Shrewsbury.

SLOUGH, BUCKINGHAMSHIRE. UPTON HOSPITAL. SENIOR HOUSE OFFICER (casualty) required, working with Casualty Registrar in busy Casualty Department. Experience given in plastic and orthopædic cases.

Applications, with names of 2 referees, to Secretary.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (274 Beds.) RESIDENT HOUSE SURGEON required mid-October. Pre-registration candidates eligible.

Applications, with copies of recent testimonials, should be forwarded to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (274 Beds.) RESIDENT HOUSE PHYSICIAN required. Pre-registration candidates eligible.

▸ Applications, with copies of testimonials, should be forwarded to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton, as soon as possible.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (384 Beds.) HOUSE PHYSICIAN (House Officer grade) required for 1 of the 2 medical firms for duties mainly on the acute wards. Post vacant approximately 21st October, 1957, and tenable for 6 months. Preference given to candidates seeking post under the Medical Act, 1950.

▸ Applications to Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (384 Beds.) HOUSE PHYSICIAN (House Officer grade) required for duties mainly in the Pædiatric Department. Post vacant approximately 21st October, 1957, and tenable for 6 months. Preference given to candidates seeking pre-registration post under the Medical Act, 1950.

Applications to Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. ALBANS, HERTFORDSHIRE. CELL BARNES HOSPITAL. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required at above Hospital. This is a modern hospital where 750 mental defectives of all types and ages are under care. Approved for D.P.M. Hospital may be visited by direct appointment.

Application forms obtainable from the Group Secretary, Harperbury Hospital, St. Albans, Herts, and returnable by 5th October, 1957.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time SENIOR REGISTRAR in Psychiatry for duty at St. Francis Hospital, Haywards Heath, Sussex, and in the mental observation ward of the Brighton General Hospital. Candidates should possess an appropriate higher qualification and have had adequate experience in general medicine. The appointment, which is renewable annually, will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales).

Applications, giving particulars of age, education, qualifications, and experience with relevant dates, together with the names and addresses of 3 referees, should be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 5th October, 1957.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Orthopædic Surgery to fill a vacancy in the approved trainee establishment at the Dartford Group of hospitals for duties mainly at West Hill Hospital. The appointment, which will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance, will be recognised for the F.R.C.S.

Applications, giving particulars of age, qualifications, and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 5th October, 1957.

STOCKPORT. CHERRY TREE HOSPITAL. (Isolation—96 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER, vacant now. This Hospital is associated with Manchester University for the study of Infectious Diseases, and the successful candidate will have ample opportunity for study.

Applications, with full particulars and copies of 2 recent testimonials, to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport, Cheshire.

SULLY HOSPITAL, Sully, Glamorgan. Regional Thoracic CENTRE. (324 Beds.) SENIOR HOUSE OFFICER (surgical) required. Experience will be gained in investigation and treatment of chest and heart conditions.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

STOKE-ON-TRENT. ORTHOPÆDIC HOSPITAL, HARTSHILL, STOKE-ON-TRENT. (78 Beds.) SENIOR HOUSE OFFICER (orthopædics) required. Post vacant very shortly. Duties also at North Staffordshire Royal Infirmary.

Detailed applications, with copy testimonials, to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. SENIOR HOUSE OFFICER (general surgery) required. Recognised for F.R.C.S. Post vacant now. 6 months appointment.

Detailed applications, with copy testimonials, to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. GYNÆCOLOGY DEPARTMENT. SENIOR HOUSE OFFICER required. Post vacant shortly. Recognised for M.R.C.O.G. (surgery). Experience in abnormal obstetrics available, but the work is mainly gynæcological.

Detailed applications, with copy testimonials, to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. (455 Beds.) SENIOR HOUSE OFFICER (orthopædics) required. Post vacant very shortly. Some duties also at Hartshill Orthopædic Hospital (78 Beds).

Detailed applications, with copy testimonials, to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. SENIOR HOUSE OFFICER (obstetrics and gynæcology) required, post vacant mid-November. Recognised M.R.C.O.G. and D.Obst.R.C.O.G.

Detailed applications, with copy testimonials, to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent, as soon as possible.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. (815 Beds.) HOUSE OFFICER (general surgery) required, vacant now. Pre-registration post. Hospital recognised for F.R.C.S.

Detailed applications, with copy testimonials, to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER in Anæsthetics. Previous anæsthetic experience desirable, but not essential. The post offers experience in anæsthesia for all types of general surgery, thoracic and cardiac surgery, including an Obstetric Unit of 60 Beds. Staff includes a Senior Registrar who shares in emergency duties.

Applications, with copy testimonials, to the Group Secretary, Stoke-on-Trent, Hospital Management Committee, Princes-road, Stoke-on-Trent.

SKIPTON (near). GRASSINGTON HOSPITAL. (206 Beds.) SENIOR HOUSE OFFICER required for the above Hospital, which provides treatment for tuberculous patients, men and women. Accommodation available for single applicants.

Applications to Medical Superintendent.

SUTTON AND CHEAM HOSPITAL, Cotswold-road, SUTTON, SURREY. RESIDENT SENIOR HOUSE OFFICER (Casualty Officer). Post recognised for F.R.C.S. Vacant 1st November.

Applications, stating age, qualifications and experience, with copies of recent testimonials and the names of 2 referees, to the Group Secretary, St. Heller Hospital, Carshalton, Surrey.

SWINDON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. ST. MARGARET'S HOSPITAL, STRATTON. Applications invited for the post of RESIDENT SENIOR HOUSE OFFICER for Pædiatric Unit. Post recognised for D.C.H., permits time for postgraduate study ; vacant 6th October.

Full details, with names of 3 referees, to Secretary, 7, Okus-road, Swindon, Wilts, as soon as possible.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. RESIDENT MEDICAL REGISTRAR required.

Application forms from, and returnable to, Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor, by 5th October.

TORQUAY. TORBAY HOSPITAL. Resident Senior HOUSE OFFICER (surgery) required immediately. Post recognised for F.R.C.S. There is a complement of 6 Resident House Officers.

Applications, stating qualifications, age, nationality, with copy testimonials (quoting Ref. F.955/83), to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

TREDEGAR GENERAL HOSPITAL, Monmouthshire. RHYMNEY AND SIRHOWY VALLEYS HOSPITAL MANAGEMENT COMMITTEE. RESIDENT SURGICAL OFFICER (Junior Hospital Medical Officer grade) required for Surgical Unit at above Hospital. Duties are those of Assistant to General Surgeon ; staff includes also House Surgeon. Commodious family flat.

Apply, with full particulars and stating names of 2 referees, to Secretary.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL, PEMBURY. Applications invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer). Post vacant 1st November, 1957. The post is tenable for 12 months in the first instance and recognised for the D.A. and the F.F.A.R.C.S.

Apply, stating age, qualifications, and experience, together with 3 testimonials, to Group Secretary, Sherwood Park, Pembury-road, Tunbridge Wells.

WARWICK (near). CENTRAL MENTAL HOSPITAL. (1400 Beds.) SENIOR HOUSE OFFICER. Neurosis Unit, adult and child psychiatry clinics, departments of electroencephalography, occupational therapy, psychology and social work. Recognised for D.P.M. Flat available.

Applications, with names and addresses of 3 referees, to Medical Superintendent within 14 days.

WHITEHAVEN HOSPITAL, Cumberland. (119 Beds, plus 31 Beds in Annexe.) HOUSE SURGEON, with orthopædic and casualty duties. Recognised pre-registration. Senior House Officer grade if appropriate. Vacant end of September.

Detailed application, with dates, and names of 2 referees, to Group Secretary, Workington Infirmary, Cumberland.

WHITEHAVEN HOSPITAL, Cumberland. (119 Beds plus 31 Beds in Annexe.) Locum JUNIOR HOSPITAL MEDICAL OFFICER SURGEON required 7th October–13th December, 1957. Duties similar to those of Surgical Registrar in a busy general hospital offering considerable operating experience in both emergency and elective surgery. Salary in accordance with national agreement.

Detailed applications, with names of 2 referees, to Group Secretary, Workington Infirmary, Cumberland.

WORCESTER (near). POWICK HOSPITAL. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER (resident or non-resident). The post offers experience in all branches of psychiatry, including all forms of modern treatment and outpatient clinics. The Hospital has a high admission-rate, is recognised for the D.P.M., and has associated Child Guidance Clinics and a Mental Deficiency Institute similarly recognised. Arrangements are made for Medical Officers to attend at the Birmingham Medical School for instruction in neurology.

Applications, with full details and the names of 2 referees, to be forwarded to the Medical Superintendent.

WREXHAM. WAR MEMORIAL HOSPITAL. (230 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER in the Orthopædic Department of the above Hospital. The post is a residential one and affords particular facilities for postgraduate study. Successful applicant will be allowed to attend for 2 days a month at the Robert Jones and Agnes Hunt Orthopædic Hospital, Oswestry. The Hospital is recognised for the Diploma of F.R.C.S. (Eng. and Edin.).

Applications, stating age, nationality, qualifications, and experience, together with copies of 2 recent testimonials, to be addressed to the Group Secretary, Maelor General Hospital, Wrexham, as soon as possible.

WELSH REGIONAL HOSPITAL BOARD.

REGISTRAR (obstetrics and gynæcology), Maelor General (591 Beds) and War Memorial Hospital (230 Beds), Wrexham (total of 60 obstetric and gynæcology beds) ; and Trevalyn Maternity Hospital, Rossett, near Wrexham (45 Beds). Resident.

REGISTRAR (psychiatry), Morgannwg Hospital, Bridgend (all modern treatments, active outpatient clinics, Child Guidance Clinic, and Psychological Department). Within easy reach of University of Wales. Accommodation available.

REGISTRAR (general surgery) to serve Caernarvon and Anglesey Hospital Management Committee. Based at Llandudno General Hospital. Hospital recognised for F.R.C.S. Non-resident.

REGISTRAR (pædiatrics). Based Merthyr General Hospital, Merthyr, to serve Merthyr and Aberdare Hospital Management Committee.

REGISTRAR (pædiatrics), Morriston Hospital, Morriston, near Swansea. Resident.

REGISTRAR in General Medicine, Morriston Hospital, Morriston, near Swansea. Resident.

REGISTRAR (traumatic surgery). Based at St. David's Hospital, Cardiff (606 Beds).

Subject to review end of first year.

Application forms from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 14 days.

WELSH REGIONAL HOSPITAL BOARD.

REGISTRAR (general medicine), Bridgend General Hospital, Bridgend (381 Beds). Hospital recognised for major diplomas. Resident/non-resident.

REGISTRAR (psychiatry), St. David's Hospital, Carmarthen (1000 Beds). All modern forms of treatment carried out. Extensive outpatient service undertaken. Hospital recognised for training for D.P.M. Flat available.

PÆDIATRIC REGISTRAR, Maelor General Hospital, Wrexham (591 Beds). Unit consists of 50 general pædiatric beds, also care of neonates. Recognised for D.C.H. Resident.

REGISTRAR (general medicine). Based at Caerphilly District Miners' Hospital, Caerphilly.

Subject to review end of first year.

Application forms from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 14 days.

WATFORD AND DISTRICT PEACE MEMORIAL HOSPITAL. (208 Beds.) Applications are invited for the post of CASUALTY OFFICER (Senior House Officer), vacant October. Post recognised for F.R.C.S. Salary according to National Health scale.

Apply, with copies of 2 testimonials, to the Administrator, Peace Memorial Hospital, Watford, Herts.

WATFORD CHEST CLINIC, Peace Memorial Hospital, WATFORD. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications invited for the post of REGISTRAR at the above Clinic and associated beds (tuberculosis 47, chest medicine 16) at Shrodells and Holywell Hospitals. This is a new Chest Clinic. Experience in general medicine and tuberculosis work, including refill techniques, is essential. This chest unit is closely associated with Harefield Hospital, the Physician-in-charge being on the Consultant staff of this Hospital. Applicants invited to visit the clinic and should contact the Physician-in-charge.

Application form obtainable from, and returnable to, the Secretary, West Herts Group Hospital Management Committee, 9, Rickmansworth-road, Watford, Herts, by not later than 10 days after the appearance of this advertisement.

WATFORD CHEST CLINIC, Peace Memorial Hospital, WATFORD. Locum REGISTRAR required immediately for work at the above Chest Clinic and beds (tuberculosis and chest medicine) at associated hospitals. Experience of refills essential. Car is desirable and allowances are paid.

Apply immediately to the Physician-in-charge (Telephone : Watford 9266).

WATFORD. GROUP 9 PATHOLOGICAL LABORATORY. Applications are invited for the post of NON-RESIDENT PATHOLOGIST (Senior House Officer grade). The appointment is tenable for 1 year in the first instance. A special interest in morbid anatomy is desirable.

Applications, with names of 3 referees, should be sent to Consultant Morbid Anatomist, Group 9 Laboratory, 6, Rickmansworth-road, Watford.

WEST HARTLEPOOL. GENERAL HOSPITAL. (471 Beds.) HARTLEPOOLS HOSPITALS MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE PHYSICIAN (pre-registration) or SENIOR HOUSE PHYSICIAN at the above Hospital, vacant early October.

Applications, stating age, nationality and qualifications with dates, and accompanied by copies of 2 testimonials, should be sent to the Group Secretary at the General Hospital, West Hartlepool, as soon as possible.

YORK. FAIRFIELD SANATORIUM (68 Beds), CITY HOSPITAL (256 Beds) AND COUNTY HOSPITAL (266 Beds). Required in December, 1957, SENIOR HOUSE OFFICER in Chest Diseases and General Medicine (non-resident) to spend half time at Fairfield Sanatorium and at the City Hospital where 8 beds are reserved for investigation of chest cases, and at the Chest Clinic where outpatient refill clinics are held, and remainder of time at the County and City Hospitals in the Department of General Medicine. Previous experience in treatment of tuberculosis an advantage.

Applications, giving age, nationality, experience, qualifications and names of 2 referees, to Group Secretary, York A and Tadcaster Hospital Management Committee, Bootham Park, York.

WIGAN. ROYAL ALBERT EDWARD INFIRMARY. REGISTRAR in Radiodiagnosis required for duties mainly at the Royal Albert Edward Infirmary, Wigan (resident or non-resident). Post now vacant. Applicants should preferably hold the D.M.R.(D.).

Applications to Secretary, Wigan Infirmary.

WIGAN. ROYAL ALBERT EDWARD INFIRMARY. SENIOR HOUSE OFFICER for duty in the Pædiatric Department at Wigan Infirmary, and also to undertake neonatal work at Billinge Hospital. Post recognised for D.C.H. Consultant Pædiatrician-in-charge. Post vacant early October.

Applications, with names of 2 referees, to the Secretary, Royal Albert Edward Infirmary, Wigan.

SOUTH AFRICA. DONALD FRASER HOSPITAL, SIBASA, NORTHERN TRANSVAAL. Applications are invited for the post of ASSISTANT MEDICAL OFFICER in the above Mission Hospital. Applicants must be interested in the physical and spiritual welfare of the African staff and patients. Salary scale £825–£75–£900–£100–£1000–£50–£1250, plus £200 cost-of-living allowance. Previous experience will be taken into consideration in determining commencing salary. The Hospital has 180 Beds and is planning to add another 100 beds for patients suffering from tuberculosis. There are 2 well-equipped operating theatres and an X-ray plant.

Applications, giving details of age, experience and qualifications, together with the names and addresses of 2 referees, should be addressed to the Medical Superintendent, Donald Fraser Hospital, P.O. Vhufuli, Via Sibasa, Northern Transvaal, South Africa.

U.S.A. CAMBRIDGE, MASSACHUSETTS. Applications are invited for the positions of RESIDENCIES in Anesthesia for a 2-year period beginning 1st July and 1st September, 1957. Salary $1800 first year and $3600 second year and full maintenance. Training in all branches of anesthesia. Affiliation with other hospitals.

Applications, stating age, nationality, qualifications, and experience, together with the names of their referees, should be forwarded to the Director of Anesthesiology, P.O. Box 89, Cambridge, Massachusetts. Travelling expenses to and from the U.S.A. will be paid. Particulars will be sent as soon as application is received. Please enclose recent photograph with application.

U.S.A. JEWISH CHRONIC DISEASE HOSPITAL, 86, East 49th-street, BROOKLYN 3, NEW YORK. RESIDENCIES, Clinical Pathology; first or second year level. 500-Bed active research hospital. 200,000 procedures annually. Includes steroid chemistry, radio-isotopes, hormone assays. Stipend—open. Full maintenance.

Apply: Executive Director.

Public Appointments

BASUTOLAND AND SWAZILAND PROTECTORATES. MEDICAL OFFICERS with qualifications registrable in United Kingdom required for general duties. Appointment on 2 years probation to the pensionable establishment. Salary £940–£1515 a year, starting point determined by age and experience. Following also payable:—

(*a*) Cost-of-living allowance of 15½% of salary up to maximum of £170 10s. a year for married officers and half this rate for single officers.

(*b*) Education allowance of £50 for each child (up to 3 under the age of 18) for education outside territory. This allowance is about to be increased.

Free passages for Officer, wife, and up to 3 children. Local leave permitted and generous home leave granted after each tour of 36 months. Income-tax at low local rates.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting No. BCD. 117/76/01).

BECHUANALAND PROTECTORATE. Medical Officers with qualifications registrable in United Kingdom required for general duties. Appointment can be either on 2 years probation to pensionable establishment or on 30 months contract with gratuity (taxable) of 12½% of aggregate emoluments. Salary scale £940–£1515 a year, starting salary determined by age and experience. Following non-pensionable allowances are payable:—

(*a*) Cost-of-living allowance 15½% of salary up to maximum of £170 10s. a year for married officers and half this rate for single officers.

(*b*) Special allowance of £60 a year for married officers and £30 for single officers.

(*c*) Education allowance of £50 for each child (up to 3 under the age of 18) for education outside territory. This allowance is about to be increased.

Private practice permitted varying from station to station.

Quarters and heavy furniture provided at low rental. Free passages for Officer, wife, and up to 3 dependent children. Local leave permitted and generous home leave granted after each tour. Income-tax at low local rates.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting No. BCD. 117/76/02).

FACTORY DOCTORS. Factories Acts, 1937 and 1948. The following appointment as Appointed Factory Doctor is vacant. Apply to Chief Inspector of Factories, 19, St. James's-square, London, S.W.1.

District	*County*	*Latest date for receipt of applications*
BEDWORTH	WARWICK	5TH OCTOBER, 1957

PLYMOUTH. CITY OF PLYMOUTH. Assistant Medical OFFICER OF HEALTH AND SCHOOL MEDICAL OFFICER. Applications invited for the above superannuable post from registered medical practitioners, Male or Female, with at least 3 years experience since qualification. D.P.H. or D.C.H. desirable. Salary scale £1050–£50–£1200–£55–£1475 p.a. Appointment terminable by 3 months notice on either side. The work will be primarily in the School Health and Maternity and Child Welfare Departments but other duties of a general public health nature may be allocated by the Medical Officer of Health.

Forms of application not provided. Applications to the undersigned stating age, marital state, qualifications, and experience, together with the names and addresses of 2 referees, not later than 30th September, 1957.

T. PEIRSON, Medical Officer of Health.

"Seven Trees," Lipson-road, Plymouth.

GOVERNMENT OF THE EASTERN REGION OF NIGERIA. SPECIALIST (Gynæcologist) required to undertake clinical gynæcology and obstetrics including visits to hospital units in the Region when convenient, and advising medical officers in obstetrics and gynæcology. Candidates must possess registrable medical qualifications, M.R.C.O.G., or equivalent, and have considerable experience. Appointment on contract for 2 tours of not more than 2 years each. Salary £2442 a year with gratuity (taxable) on completion of satisfactory engagement at rate of £37 10s. for each completed period of 3 months service (including leave). Quarters provided at rental of 10% of salary. Taxes at local rates. Annual local leave; generous home leave after each tour. Free return passages for Officer and wife; and, when appropriate, either (but not both) of the following in any 1 tour:—

(*a*) 1 return sea passage for each of 2 children under age 18 subject to maximum of £75 for the return journey for each child, or

(*b*) An allowance of £75 a year for each of 2 children under age 18 maintained outside Nigeria for the whole tour.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting No. BCD. 117/411/017).

GOVERNMENT OF THE EASTERN REGION OF NIGERIA. SPECIALIST (Pathologist) required to organise and run a Regional Laboratory Service, take charge of a Regional Laboratory when built, and administer subsidiary laboratory units attached to Government hospitals in the Region. Candidates must possess D.C.P. or M.D. (London) in Pathology. Appointment on contract for 2 tours of not more than 2 years each. Salary £2442 a year, and gratuity (taxable), payable on completion of satisfactory engagement, of £37 10s. for each completed period of 3 months service (including leave). Quarters provided at rental of 10% of salary. Taxes at local rates. Annual local leave permissible; generous home leave after each tour. Free return passages for Officer and wife; and, when appropriate, either (but not both) of the following in any 1 tour of service:—

(*a*) 1 return sea passage for each of 2 children under age 18 subject to maximum of £75 for the return journey for each child, or

(*b*) An allowance of £75 a year for each of 2 children under age 18 maintained outside Nigeria for the whole tour.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting No. BCD. 117/411/019).

HER MAJESTY'S OVERSEAS CIVIL SERVICE. Uganda. PATHOLOGIST required to work in the Medical Laboratory under the Senior Pathologist. Duties include teaching pathology, forensic medicine, and hæmatology. Candidates must possess medical qualifications registrable in the United Kingdom. Appointment on permanent basis with pension (non-contributory and salary £1284–£2115 a year; or on short-term contract, with gratuity, and salary £1503–£2115 a year. Salary starting point determined by qualifications and experience. Gratuity (taxable) for contract service is 13½% of total salary drawn excluding allowances. Pension at rate of 1/600th of final pensionable emoluments for each completed month of service. Candidate in National Health Service may retain superannuation rights up to 6 years and receive gratuity (taxable) of 20% of salary after engagement. Only permanent officer can be a member of Her Majesty's Overseas Civil Service. Quarters at low rental. Items of hard furniture supplied at additional rental. Free passages in both directions; for Officers serving tour of 30–36 months, 4 air passages for Officer, wife, and dependent children or sea passages up to cost of 3 adult fares. Educational subsidies are payable, which vary from £90 a year (or half the school fees, whichever is less), for primary education, to £140 a year (or three fifths of school fees, whichever is less) for secondary education of first child. An additional £9 payable for second child and £18 for third and subsequent children attending school at the same time (all subject to three-fifths fee not being less than subsidy). Education facilities are available in East Africa, though many parents send children home to United Kingdom for secondary education. Income-tax at local rates. Local leave permissible and generous home leave granted after each tour.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting No. BCD. 117/9/018).

HER MAJESTY'S OVERSEAS CIVIL SERVICE. BAHAMAS. Applications invited from doctors with qualifications registrable in United Kingdom for appointment as ASSISTANT MEDICAL OFFICER in the Princess Margaret Hospital in Nassau or as DISTRICT MEDICAL OFFICER in 1 of the Out Islands. Candidates must be prepared to serve anywhere in the Bahamas. Appointment on permanent basis with pension or on agreement for 3 years. (Only permanent officers are members of Her Majesty's Overseas Civil Service.) Salary £1400 a year. No income-tax at present. Free quarters if posted to the Out Islands or rent assistance if posted to New Providence. Private practice permitted in Out Islands. Free passages for Officer, wife, and up to 2 children on appointment. Free return passages if appointed on agreement. Baggage allowance up to £40 payable on excess baggage. Generous leave. Healthy climate. Excellent social and recreational facilities.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting No. BCD. 117/27/02).

REPUBLIC OF THE SUDAN. The Ministry of Health invite applications for the post of Male SPECIALIST CHEST PHYSICIAN. Candidates must possess necessary qualifications for the post, viz., M.R.C.P. Age 28–45. Appointment will be on a short-term contract (with bonus for 3 years). Salary scale ranges from £S.1750 to £S.2210 for Junior Consultants and £S.2330 for Full Consultants. Starting pay will be fixed according to age, qualifications, and experience of the candidates. A cost-of-living allowance is payable and an outfit allowance of £S.50.

Further information and application forms obtainable from Sudan Embassy, Personnel Section, Cleveland-row, St. James's, S.W.1, quote reference Chest Specialist 4/1203. Closing date 15th October, 1957.

NAVY, ARMY AND AIR FORCE INSTITUTES. Applications are invited from general practitioners in the undernoted towns for the appointment in a part-time capacity as MEDICAL OFFICERS to this Corporation. Successful applicants would be required to examine and report on the condition of employees of the Corporation who may be referred to them from time to time. Fees for this work will be paid on a scale agreed with the British Medical Association.

Applications, giving details of qualifications and experience, should be sent to the Chief Medical Officer, Navy, Army and Air Force Institutes, Kennington-lane, London, S.E.11, not later than 5th October, 1957.

The towns for which applications are invited are :—

KINGS LYNN	PETERBOROUGH	LINCOLN
LEICESTER	NOTTINGHAM	GRIMSBY

PERTH AND KINROSS JOINT COUNTY COUNCIL invite applications for the post of ASSISTANT MEDICAL OFFICER (Female). Duties mainly School Health. D.P.H. or D.C.H. an advantage. Salary scale £1050–£1475 with placing according to experience.

Particulars and forms of application from the County Clerk, P.O. Box 15, County Offices, York-place, Perth. Applications to be lodged by 30th September, 1957.

WARWICKSHIRE COUNTY COUNCIL. County Medical OFFICER OF HEALTH'S DEPARTMENT. Applications are invited from registered medical practitioners for the permanent appointment of ASSISTANT COUNTY MEDICAL OFFICER OF HEALTH (Male or Female). Preference will be given to those holding the D.P.H. or D.C.H. and with previous experience. Conditions of service and salary (£1050–£1475) will be in accordance with the Whitley Council. The successful candidate will be required to provide a motor-car in the performance of duties, for which Whitley Council scale allowances are payable.

Further particulars, including details of area and duties, and application forms may be obtained from the County Medical Officer of Health, Shire Hall, Warwick. Closing date for applications is 12th October, 1957.

L. EDGAR STEPHENS, Clerk of the Council.

Shire Hall, Warwick, 4th September, 1957.

WARWICK. COUNTY OF WARWICK. Borough of NUNEATON, URBAN DISTRICT OF BEDWORTH AND RURAL DISTRICT OF ATHERSTONE. Applications are invited from suitably qualified medical practitioners for the combined appointments of MEDICAL OFFICER OF HEALTH for the Borough of Nuneaton, the Urban District of Bedworth, and the Rural District of Atherstone. The successful candidate will also be appointed Area Medical Officer for Health and School Medical Services under the Warwickshire County Council for the same area. Aggregate inclusive salary £2066 5s. rising to £2473 2s. 6d. p.a.

Further particulars and conditions of appointment obtainable from the Town Clerk, Council House, Nuneaton. Closing date for applications 30th September, 1957.

WESTMINSTER CITY COUNCIL AND HOLBORN BOROUGH COUNCIL. Joint appointment of DEPUTY MEDICAL OFFICER OF HEALTH (permanent superannuable post). Salary £2050–£105–£2365 p.a. Applicants to be registered medical practitioners and to hold a registered Public Health qualification; age under 46 years at 30th September, 1957. The person appointed will act as Deputy Medical Officer of Health for the 2 boroughs. His services will be allocated in the proportion of three-fourths to Westminster and one-fourth to Holborn.

Applications (marked "Deputy Medical Officer of Health"), stating age, war service, qualifications, present and past appointments, with names of 3 referees, to the Town Clerk, Westminster City Hall, Charing Cross-road, London, W.C.2, by 11th October, 1957.

YORKSHIRE. NORTH RIDING COUNTY COUNCIL. Applications are invited from suitably qualified medical practitioners for whole-time mixed appointment of MEDICAL OFFICER OF HEALTH to Guisborough, Loftus and Skelton, and Brotton Urban District Councils and ASSISTANT COUNTY MEDICAL OFFICER to take up duty 1st April, 1958. Salary £1628 1s. 2d., rising by annual increments to £2021 6s. 1d. p.a. Conditions of service in accordance with Whitley Councils recommendations (Medical Council Committee "C"). House available. Medical examination necessary.

Further particulars and forms of application obtainable from the Clerk of the County Council, County Hall, Northallerton, should be returned within 14 days from the appearance of this notice.

General Practice

For an **Executive Council post** *(England and Wales) apply on form* **E.C.16A** *obtainable from the council. Mark envelope "Vacancy."*

GRASMERE. Applications are invited for vacant Rural Practice. List of approximately 500 dispensing patients only. Apply on Form E.C. 16A (obtainable on request) within 14 days of this advertisement. W. TOWNLEY COTTAM, Clerk,

60 Highgate, Kendal. Westmorland Executive Council.

OXFORD. Applications are invited for Vacancy (City of Oxford) due to death. List as at 1st July, 1957—5098. Position regarding house and surgery accommodation not yet clarified. Apply by 19th October, 1957, on Form E.C.16A to—

V. R. PARRY,

Clerk of the Oxford County and City Executive Council.

73, George-street, Oxford.

SILLOTH, CUMBERLAND. Applications are invited for VACANCY (mixed urban and rural) owing to resignation of practitioner. List at present date approximately 2142. Intermediate area. Residence and surgery available. Apply on Form E.C.16A by 27th September, 1957, to—

F. M. SMITH, Clerk to Cumberland Executive Council.

7, Chatsworth-square, Carlisle.

Miscellaneous

British Overseas Airways Corporation require a Medical Officer in the Corporation's Medical Service. Applicants should be between 28 and 34 years of age, with good academic qualifications and should possess a sound standard of clinical medicine. R.A.F. experience in the medical care of aircrew will be an advantage. The successful applicant will be based at London Airport, and the work will primarily consist of clinical examinations of flying staff and general medical duties in connection with the Corporation's Medical Service and will involve flying at home and overseas. Commencing salary will be in the range of £1785–£2170 p.a. according to age, qualifications and experience. The successful candidate will be required to join the Corporation's pension scheme.

Applications should be made, together with details of professional qualifications and experience to the Chief Personnel Officer, B.O.A.C. Headquarters, London Airport, Hounslow, Middlesex. The closing date for receipt of applications will be 11th October, 1957.

British European Airways invite applications for 2 medical posts of Assistant Medical Officer in the Corporation's Medical Service, based in United Kingdom. Applicants (Male) must be between 30 and 40 years of age and hold a British medical registration. Preference will be given to candidates with experience of aviation medicine or general practice. Commencing salary according to experience will be within the current B.M.A. range for the post (£1400–£1700). Initially the posts will be temporary appointments for 12 months but successful candidates will be eligible for consideration for a permanent appointment after the satisfactory completion of this period, which will require membership of the Corporation's pension scheme.

Application forms can be obtained from the Establishments Officer, Personnel Dept., B.E.A., Keyline House, Ruislip, Middx., to whom they should be returned, together with a recent photograph, by 14th October, 1957.

Rhokana Corporation Limited, Northern Rhodesia. A Medical Officer is required for Rhokana Corporation Mine Medical Service at Kitwe, Northern Rhodesia. There is a vacancy for a Medical Officer with an advanced qualification in medicine, preferably one who has had experience as Registrar. He will work under the Chief Medical Officer in association with the Physician already employed by the Corporation. His duties will include the care of patients in the Corporation's hospitals (European and African) under the direction of the Specialist Physician, the holding of clinics, and some general practice. The Corporation employs 10 medical practitioners inclusive of the above-mentioned. Salary is at the rate of £1700 p.a., part of which is deemed to be in lieu of private practice. A modern house of bungalow type will be available immediately at a nominal rental. Water is free and the charges for light are low. A motor-car is provided free for use within the Corporation's area. There is a contributory pension scheme and a variable bonus is payable, dependent on the selling price of copper. Holiday leave is at the rate of 51 days p.a. accumulative up to a maximum of 153 days. The Corporation pays the cost of the outward passage of the successful applicant and wife and family.

Application forms can be obtained from Rhokana Corporation Limited, 40, Holborn-viaduct, London, E.C.1.

Sudbury, Ontario, Canada. G.P. requires young partner with obstetric experience, for expanding town. Higher qualification desirable. $700 per month starting salary. No capital. —Reply, full details, Address, No. 332, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Typewriting and Duplicating. First-class work at moderate prices by experienced medical typists. Electric machines. —SYBIL RANG, 21, Heath-street, Hampstead, London, N.W.3 (HAM 5329/0504).

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimens of urine and £1 1s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

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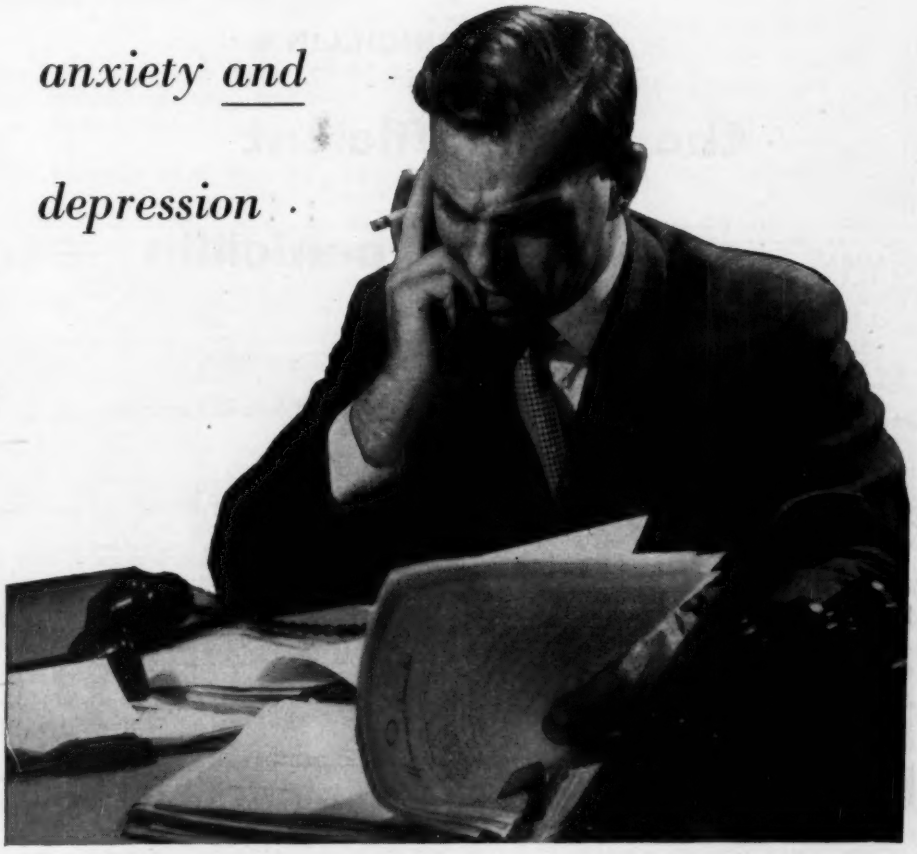

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